Synthetic Studies of Rifamycins. II.[1] Syntheses of Methyl 2,4,6,7-Tetradeoxy-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-heptopyranosid-6-ulose and Its Derivatives Utilizable in the Construction of the Rifamycin Ansa Chain Portion

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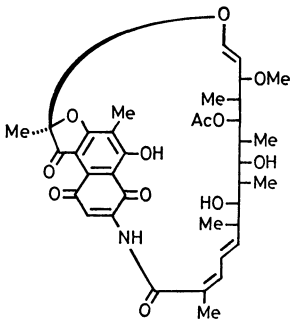
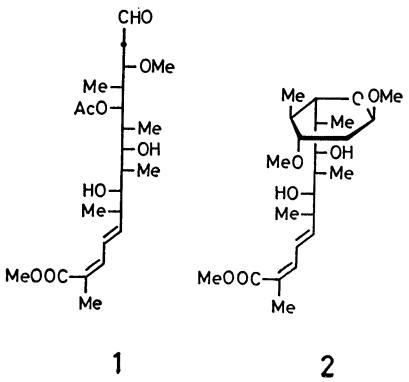
3,6-Dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactopyranose(**12**) was prepared in 10 steps from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside. **12** was converted into 4,5-di-*O*-acetyl-3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactose, which was then condenced in ether with (methoxymethylene)triphenylphosphorane (generated from the phosphonium salt with the dimethylsulfinylmethanide anion in ether) to produce 5,6-di-*O*-acetyl-2,4,7-trideoxy-4-*C*-methyl-1,3-di-*O*-methyl-D-*galacto*-1-enoheptitol (**16**). The treatment of **16** with NBS in methanol, followed by the debromination of the resulting 2-bromo aldehyde dimethyl acetal with tributylstannane, deacetylation, and mild methanolysis afforded methyl 2,4,7-trideoxy-4-*C*-methyl-3-*O*-methyl-β-D-*galacto*-heptopyranoside(**19**), which then provided the title compound **20** upon Jones oxidation. The potential intermediates, the 1-lithio-1-(methyl 2,4-dideoxy-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-pentopyranos-5-yl)ethene and (*E*)-2-(methyl 2,4-dideoxy-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-pentopyranos-5-yl)propenylcopper intermediates, were prepared from **20** *via* the corresponding alkenyl iodide and (methyl 2,4-dideoxy-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-pentopyranos-5-yl)ethyne and were demonstrated to condense with benzaldehyde and ethylene oxide respectively.

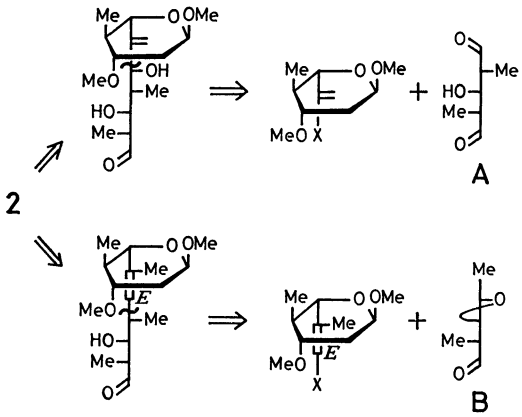
Rifamycins are the first natural compound with an aromatic ring system spanned by a long aliphatic bridge,[2] called the ansa chain. The aliphatic chain compound, **1**, corresponding to the intact ansa chain present in rifamycin B, O, S, and SV has thus far been neither isolated from a natural source nor synthesized. Corey[3] has recently reported the highly stereoselective synthesis of some fragment intermediates for the elaboration of the ansa-chain portion of rifamycins. In the course of our synthetic studies of rifamycins, the new ansa-chain compound, **2**, the deacetylated cyclic methyl acetal derivative of **1**, has been isolated[1] on the novel degradation of 25-deacetylrifampicin. We have been interested[4] in the synthesis of the rifamycin ansa chain in the form of **2**, which is considered to be a useful intermediate in the synthesis of rifamycin. This paper deals with the synthesis of methyl 2,4,6,7-tetradeoxy-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-heptopyranosid-6-ulose (**20**), a viable synthetic intermediate containing the cyclic methyl acetal moiety of **2**, and with its conversions into the potential intermediates, **23** or **26**, utilizable in the coupling reaction with the second synthetic segments, such as **A** or **B**, with the aldehydic or epoxidic functionality (Scheme 1).



Rifamycin S



1 2

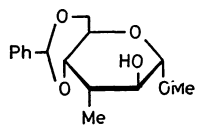


Scheme 1.

Results and Discussion

The starting material, methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside(**3**),[5-7] could be obtained on a large scale from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside[8] and methylmagnesium chloride by the method of Inch and Lewis.[7] The conversion of **3** into methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-glucopyranoside(**5**) was accomplished *via* the inverted keto sugar, **4**, according to

the procedure of Inch *et al.*[9] in a 74% overall yield. The *O*-methylation of **5** with sodium hydride and methyl iodide in DMF gave **6** in a 73% yield. The treatment of **6** with *N*-bromosuccinimide (NBS)



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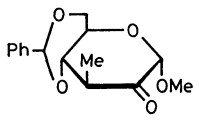

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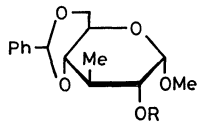
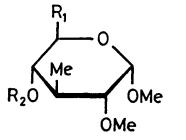
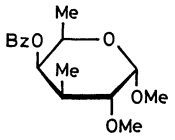


5 R = H
6 R = Me

in boiling carbon tetrachloride,[10] followed by the lithium aluminium hydride reduction of the bromo derivative, **7**, afforded methyl 3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α-D-glucopyranoside(**8**) in a 65% yield. The *O*-mesylation of **8** with mesyl chloride in pyridine, followed by the treatment of the resulting 4-mesylate, **9**, with sodium benzoate in DMSO at 120 °C, gave the inverted benzoate **10** in a 61% overall yield from **8**. The acetolysis of **10** with acetic anhydride in the presence of concd sulfuric acid afforded **11** as an anomeric mixture in a 76% yield. The hydrolysis of **11** with sodium hydroxide gave 3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactose(**12**) in a 92% yield. In preparative runs, compound **12** could be obtained in about a 32% overall yield from **3** without any isolation of the intermediates (**4**—**11**).



7 R_1 = CH_2Br, R_2 = Bz
8 R_1 = Me, R_2 = H
9 R_1 = Me, R_2 = Ms



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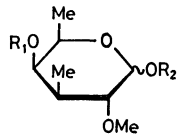
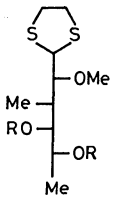
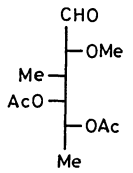


11 R_1 = Bz, R_2 = Ac
12 R_1 = R_2 = H

The conversion of **12** into **19** in a moderate overall yield (23%) was accomplished through the following eight steps. The dithioacetalization of **12** with 1,2-ethanedithiol and concd hydrochloric acid, followed by acetylation with acetic anhydride and 4-dimethylaminopyridine in ethyl acetate, gave **14** in a 70% overall yield. The demercaptalation of **14** with a 2:1 mixture of mercury(II) chloride and red mercury(II) oxide[11] afforded the aldehyde **15** in a 95% yield. The Wittig condensation[12] of **15** in ether with (methoxymethylene)triphenylphosphorane (prepared from the corresponding phosphonium chloride with phenyllithium in ether) yielded the enol ether, **16**, in a low yield (≈10%). When **15** was treated with the ylide in DMSO according to Corey's method,[13] no condensation product was obtained, but when **15** was allowed to react in ether with a two-fold excess of the ylide (prepared by the action of 4 M** methylsulfinylmethanide anion in DMSO[13a]) with the phosphonium chloride in ether), the desired enol ether, **16**, was obtained in a 72% yield as a 7.7:1 mixture of *E* and *Z* isomers. The direct conversion of **16** into the



13 R = H
14 R = Ac



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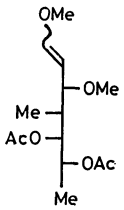
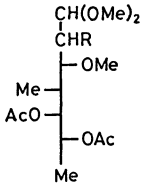
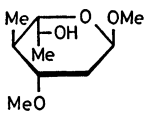


16

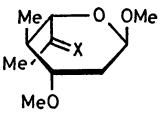
homolog of **15** by acid-catalyzed hydrolysis could not be accomplished because of the predominant formation of the α,β-unsaturated aldehyde by the elimination of the 3-methoxyl group, and so an indirect process was necessary. The treatment of **16** with NBS in methanol containing solid sodium hydrogencarbonate afforded the crystalline bromo dimethyl acetal **17** as an epimeric mixture in a 74% yield. The debromination of **17** with tributylstannane and α,α'-azobisisobutyronitrile gave **18** in a 96% yield. The deacetylation of **18** with sodium hydroxide, followed by mild methanolysis with 0.5% methanolic hydrogen chloride, afforded a 1:5 mixture of methyl 2,4,7-trideoxy-4-*C*-methyl-3-*O*-methyl-α-D-*galacto*-heptopyranoside and its β-anomer, which, after recrystallization, gave the major isomer, **19**, in a 63% overall yield from **18**. The Jones oxidation of **19** afforded the title compound, **20**, in a 93% yield.



17 R = Br
18 R = H



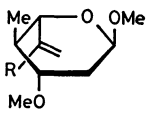
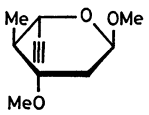
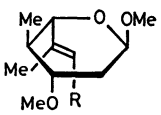
19



20 X = O
21 X = NNH_2

The methyl ketone, **20**, was converted into the alkenyl iodide, **22**, in a 72% yield *via* the hydrazone, **21**, according to the procedure of Barton *et al.*[14] The iodide, **22**, was convertible into the lithium compound, **23**, in ether by treatment with a 1—1.2 equiv of butyllithium[15] in hexane at −78 °C for 1 h. The lithium reagent, **23**, thus obtained was reacted with 1 equiv of benzaldehyde at −50 °C to give the addition product, **24**, in a 54% yield. The potential intermediate, **26**, was derived from **22**. The treatment[16] of **22** with potassium hydroxide in boiling ethanol afforded the alkyne, **25**, in a 74% yield. The alkyne **25** was subjected to an addition reaction[17] with the methylcopper complex which had been prepared from methylmagnesium bromide and a dimethyl sulfide complex of copper(I) bromide[18] in a mixture of ether and dimethyl sulfide according to the procedure reported by Marfat *et al.*[17] The reaction proceeded effectively in the same solvent system at −25 °C for 1 week, resulting in the almost exclusive formation of the alkenylcopper intermediate, **26**, as evidenced by the isolation of the 1-iodo-2-methylalkene, **27**, presumably with an *E*-configuration, in a 52% yield as the sole

** 1 M=1 mol dm^{-3}.

22 R = I
23 R = Li
24 R = CH(OH)Ph

25

26 R = Cu(Me$_2$S)MgBr$_2$ [17]
27 R = I
28 R = CH_2CH_2OH

addition product after a reaction with iodine.[19] This result indicated that the addition reaction proceeded in a stereospecific syn manner, with copper becoming associated with the terminal carbon, as in the case of simple nonfunctionalized terminal alkyne.[20] Normant *et al.*[21,22] showed that the regioselectivity of the addition of the RCu, MgX_2 reagent to terminal alkynes was affected by the presence of such heteroatom substituents as alkoxyl groups at the propargyric position in the alkyne, and mixtures of products were frequently obtained. The coordination of the hetero atom with a copper moiety has been suggested to explain the formation of products derived from alkenylcopper intermediates with copper at the internal carbon.[23] Under our reaction conditions, the copper reagent forms complexes so strongly with dimethyl sulfide present in the solvent system that the coordination of the copper moiety with the propargyric-ring oxygen atom may be out of the question. The alkenylcopper intermediate, **26**, was converted into the mixed cuprate with 1-lithiopentyne according to the procedure proposed by McGuirk *et al.*[24] and allowed to react with ethylene oxide at −25 °C for 24 h to give the homoallylic alcohol, **28**, in a 46% yield.

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 precision polarimeter. The ^{1}H NMR (PMR) spectra were determined with Varian A60 and EM-390 spectrometers, using TMS as the internal standard. Unless otherwise stated, the TLC and column chromatography were performed on silica gel Wakogel B-5 and Wakogel C-200 respectively. In general, the concentration was carried out under a reduced pressure of below 30 °C.

Methyl 4,6-O-Benzylidene-3-deoxy-3-C-methyl-α-D-arabino-hexopyranosid-2-ulose (4). A mixture of dry DMSO (54 ml), dry pyridine (5.5 ml), and trifluoroacetic acid (2.89 ml, 0.037 mol) was added to a solution of **3** (50.0 g, 0.178 mol) in dry benzene (350 ml). A solution of dicyclohexylcarbodiimide (44.2 g, 0.214 mol) in dry benzene (150 ml) was then added, drop by drop, to the mixture under ice-cooling. After the mixture had been stirred at room temperature for 7 h, the precipitates formed were filtered and washed with benzene. The filtrate and washings were combined and washed successively with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions, dried, and evaporated to afford a yellow syrup of crude methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-*ribo*-hexopyranosid-2-ulose (51.4 g). This syrup was dissolved in DMF (247 ml) containing triethylamine (23 ml). After being stored at room temperature for 3 d, the mixture was poured into ice water. The precipitates were collected by filtration, washed with water, and dried at 40 °C to afford pale yellow crystals of **4** (43.4 g, 87.5%); mp 127.5—129 °C. Recrystallization from ethyl acetate–hexane gave a pure sample of **4**: mp 130—131 °C; $[\alpha]_D^{27}$ +58° (*c* 1.26, $CHCl_3$); IR (0.122 M, CCl_4) 1750 cm^{-1}; PMR ($CDCl_3$) δ=1.21 (3H, d, 3-Me, J=5.9 Hz), 3.50 (3H, s, OMe), 4.63 (1H, s, H-1), and 5.53 (1H, s, benzylic H). Found: C, 64.87; H, 6.55%. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52%.

Methyl 4,6-O-Benzylidene-3-deoxy-3-C-methyl-α-D-glucopyranoside (5). Powdered $LiAlH_4$ (5.22 g, 0.138 mol) was slowly added to a stirred ice-cooled solution of **4** (38.4 g, 0.138 mol) in dry ether (1.0 l), and then the mixture was stirred at room temperature for 0.5 h. Ethyl acetate (300 ml) and water (0.5 l) were added to the cooled reaction mixture, and it was stirred at room temperature for 1 h. The organic layer thus separated was washed with a saturated aqueous NaCl solution, dried, and evaporated to afford **5** as colorless plates (35.7 g, 92.3%). Recrystallization from methanol–petroleum ether gave a pure sample: mp 150.5—151.5 °C; $[\alpha]_D^{23}$ +94° (*c* 1.04, $CHCl_3$); PMR ($CDCl_3$) δ=1.18 (3H, d, 3-Me, J=6.1 Hz), 1.91 (1H, d, OH, $J_{2,OH}$=11.1 Hz), 3.26 (1H, dd, H-4, $J_{3,4}$=10.7 Hz, $J_{4,5}$=4.7 Hz), 3.48 (3H, s, OMe), 4.71 (1H, d, H-1, $J_{1,2}$=3.6 Hz), and 5.51 (1H, s, benzylic H). Found: C, 64.53; H, 7.27%. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19%.

Methyl 4,6-O-Benzylidene-3-deoxy-3-C-methyl-2-O-methyl-α-D-glucopyranoside (6). Sodium hydride (17.1 g, 55% emulsion in mineral oil) was placed in a flask and washed free from the mineral oil with hexane. The flask was evacuated until the last traces of hexane were removed from the sodium hydride. Dry DMF (75 ml) was then introduced under stirring, and a solution of **5** (10.5 g, 37.5 mmol) in DMF (30 ml) was added dropwise to the stirred ice-cooled contents. After the sirring had been continued at room temperature for 1 h, methyl iodide (34.2 ml, 513.8 mmol) was added dropwise to the stirred ice-cooled mixture over a period of 20 min. After the mixture had been stirred for 1.5 h, the excess of hydride was then destroyed by the careful addition of methanol and the solvents were removed. The residue was taken up with chloroform, washed with water and a saturated aqueous NaCl solution, dried, and evaporated to afford **6** as a yellow crystalline solid (11.5 g). The recrystallization of the crude crystals of **6** from acetone–petroleum ether gave the pure sample (8.00 g, 73%): mp 121—122.5 °C; $[\alpha]_D^{27}$ +84° (*c* 1.10, $CHCl_3$); PMR ($CDCl_3$) δ=1.15 (3H, d, 3-Me J=6.1 Hz), 3.02 (1H, dd, H-2, $J_{1,2}$=3.2 Hz, $J_{2,3}$=10.0 Hz), 3.50 (6H, s, 1- and 2-OMe), 4.86 (1H, d, H-1), and 5.52 (1H, s, benzylic H). Found: C, 65.50; H, 7.49%. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53%.

Methyl 4-O-Benzyl-6-bromo-3,6-dideoxy-3-C-methyl-2-O-methyl-α-D-glucopyranoside (7). A mixture of **6** (8.00 g, 27.2 mmol), NBS (5.08 g, 28.8 mmol), and carbon tetrachloride (120 ml) containing barium carbonate (6.76 g, 34.7 mmol) was refluxed for 2h under stirring (argon atmosphere). The solids were filtered off and washed with carbon tetrachloride. The filtrate and washings were combined and washed with saturated aqueous $Na_2S_2O_3$, $NaHCO_3$, and NaCl solutions successively. The dried solution was evaporated to give **7** (10.0 g, 98.6%) as a colorless syrup which was suitable for the next synthesis. A portion of this product (50 mg) was chromatographyd on silica gel (3 g) with 20:1 benzene–ethyl acetate to afford a pure sample of **7** (39 mg, 78%): $[\alpha]_D^{28}$ +93° (*c* 0.81, $CHCl_3$); PMR ($CDCl_3$) δ=1.04 (3H, d, 3-Me, J=6.4 Hz), 3.12 (1H, dd, H-2, $J_{1,2}$=3.7 Hz, $J_{2,3}$=10.9 Hz), 3.48 and 3.57 (each 3H, each s, 1- and 2-OMe), 4.88 (1H, d, H-4, $J_{3,4}$=9.9 Hz, $J_{4,5}$=10.2 Hz), and 4.94 (1H, d, H-1). Found: C, 51.22; H, 5.46; Br, 21.66%. Calcd for $C_{16}H_{21}O_5Br$: C, 51.49; H, 5.67; Br,

21.41%.

*Methyl 3,6-Didoxy-3-*C*-methyl-2-*O*-methyl-α-*D*-glucopyranoside (8).* The crude sample of **7** (10.0 g) was dissolved in dry THF (650 ml) and cooled in an ice bath. Powdered $LiAlH_4$ (8.13 g, 215 mmol) was slowly added to the stirred solution. The resulting mixture was refluxed for 1.5 h and then cooled in an ice bath. Ethyl acetate (240 ml) and water (150 ml) were slowly added to the reaction mixture, and the resulting mixture was stirred at room temperature overnight. The mixture was filtered with a super cell, and the filter cake was washed with ethyl acetate. The combined filtrate and washings were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (7.30 g) was chromatographed on silica gel (360 g) with 1:1 benzene–ethyl acetate to afford a colorless syrup of **8** (4.0 g, 77%): $[\alpha]_D^{15}$ +159° (*c* 0.56, $CHCl_3$); PMR ($CDCl_3$) δ=1.11 (3H, d, 3-Me, J=6.2 Hz), 1.24 (3H, d, H-6, $J_{5,6}$=6.1 Hz), 2.92 (1H, dd, H-2, $J_{1,2}$=3.1 Hz, $J_{2,3}$=10.7 Hz), 3.43 (6H, s, 1- and 2-OMe), and 4.76 (1H, d, H-1). Found: C, 56.85; H, 9.32%. Calcd for $C_9H_{18}O_4$: C, 56.82; H, 9.54%.

*Methyl 3,6-Dideoxy-4-*O*-mesyl-3-*C*-methyl-2-*O*-methyl-α-*D*-glucopyranoside (9).* A mixture of **8** (4.00 g, 21.0 mmol), dry pyridine (40 ml), and mesyl chloride (2.48 ml, 32.0 mmol) was allowed to stand at room temperature for 24 h and then evaporated. The residue was taken up with ethyl acetate, washed with a saturated aqueous NaCl solution, dried, and evaporated to afford pale yellow needles of **9** (5.07 g, 90%). Some of these crystals (71 mg) were chromatographed on silica gel (2 g) with 10:1 benzene–ethyl acetate to give a pure sample (56 mg) as colorless needles: mp 81.5—83.0 °C; $[\alpha]_D^{26}$ +127° (*c* 1.67, $CHCl_3$); PMR ($CDCl_3$) δ=1.17 (3H, d, 3-Me, J=6.3 Hz), 1.32 (3H, d, H-6, $J_{5,6}$=6.0 Hz), 2.99 (1H, dd, H-2, $J_{2,3}$=10.8 Hz), 3.08 (3H, s, OMs), 3.46 (6H, s, 1- and 2-OMe), 4.16 (1H, dd, H-4, $J_{3,4}$=9.7 Hz, $J_{4,5}$=9.7 Hz), and 4.78 (1H, d, H-1, $J_{1,2}$=3.2 Hz). Found: C, 44.44; H, 7.28; S, 11.65%. Calcd for $C_{10}H_{20}O_6S$: C, 44.72; H, 7.53; S, 11.95%.

*Methyl 4-*O*-Benzoyl-3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-α-*D*-galactopyranoside (10).* A solution of **9** (105 mg, 0.391 mmol) in DMSO (5.0 ml) was heated with dried sodium benzoate (282 mg, 1.96 mmol) at 120 °C for 6 h. After being cooled to room temperature, the reaction mixture was diluted with ethyl acetate; the solids were filtered off and washed with ethyl acetate. The filtrate and washings were combined and washed with water and a saturated aqueous NaCl solution. The dried solution was evaporated, and the residue (189 mg) was chromatographed on silica gel (5 g) with 5:1 hexane–acetone to afford a syrup of **10** (102 mg, 88.6%): $[\alpha]_D^{29}$ +153° (*c* 0.59, $CHCl_3$); IR (CCl_4) 1720 cm^{-1}; PMR ($CDCl_3$) δ=1.02 (3H, d, 3-Me, J=7.3 Hz), 1.13 (3H, d, H-6, $J_{5,6}$=6.8 Hz), 3.41 (1H, dd, H-2, $J_{1,2}$=3.1 Hz, $J_{2,3}$=10.8 Hz), 3.47 and 3.50 (each 3H, each s, 1- and 2-OMe), 4.12 (1H, dq, H-5, $J_{4,5}$=1.5 Hz), 4.94 (1H, d, H-1), and 5.27 (1H, dd, H-4). Found: C, 65.42; H, 7.45%. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53%.

*1-*O*-Acetyl-4-*O*-benzoyl-3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactopyranose (11).* To a solution of **10** (5.30 g, 18.0 mmol) in acetic anhydride (197 ml), concd H_2SO_4 (1.9 ml) was added dropwise under ice-cooling. After being kept at room temperature for 0.5 h, the reaction mixture was poured into cold water (1.8 l), neutralized with solid $NaHCO_3$, and then extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual yellow-brown syrup (5.8 g) was chromatographed on silica gel (50 g) with 10:1 benzene–ethyl acetate to afford a semi-crystalline solid of **11** (4.41 g, 76.3%) as an anomeric mixture: PMR ($CDCl_3$) δ=1.10 (3H, d, 3-Me, J=6.9 Hz), 1.19 (3H, d, H-6, $J_{5,6}$=6.2 Hz), 2.10 and 2.21 (3H, each s, OAc), 3.38 and 3.54 (3H, each s, OMe), 5.64 and 6.2—6.3 (1H, each d, H-1 of β- and α-anomers, $J_{\beta\text{-}1,2}$=7.9 Hz). Found: C, 63.53; H, 6.88%. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88%.

*3,6-Didoxy-3-*C*-methyl-2-*O*-methyl-D-galactopyranose (12).* A 1 M aqueous NaOH solution (3.67 ml) was added to a solution of **11** (490 mg, 1.52 mmol) in dioxane (3.67 ml). After being kept at room temperature for 2 d, the mixture was neutralized with a 0.5 M H_2SO_4 solution and evaporated, and acetone was added to the residue. The insoluble matter was filtered off, and the filtrate was evaporated to afford crude **12** (268 mg, 100%) as a yellow syrup. A sample (60 mg) of the syrup was chromatographed on silica gel (2 g) with 1:1 benzene–ethyl acetate to give a colorless syrup of **12** (55 mg, 92%) as an anomeric mixture; PMR ($CDCl_3$) δ=1.17 (3H, d, 3-Me, J=6.2 Hz), 1.22 (3H, d, H-6, $J_{5,6}$=6.2 Hz), 3.71 (1H, dq, H-5, $J_{4,5}$=2.9 Hz), 4.62 and 5.38 (1H, each d, H-1 of two anomers, $J_{\alpha\text{-}1,2}$=4.4 Hz, $J_{\beta\text{-}1,2}$=7.9 Hz), and 3.80 (2H, s, 1- and 4-OH). Found: C, 54.27; H, 8.98%. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15%.

*3,6-Dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactose Ethylene Dithioacetal (13).* To a stirred solution of the crude **12** (1.08 g) in 1,2-ethylenedithiol (2.57 ml) was added concd HCl (0.63 ml) dropwise under ice-cooling. After being stirred at room temperature for 2 h, the reaction mixture, which showed the presence of a trace amount of **12** on TLC (1:1 benzene–ethyl acetate), was treated with additional concd HCl (1.93 ml) at room temperature for 40 min. The resulting mixture was then poured into ice water and extracted with chloroform. The extract was washed successively with saturated aqueous $NaHCO_3$ and NaCl solutions, dried, and evaporated. The residual yellow syrup (3.18 g) was chromatographed on silica gel (60 g) with 2:1 benzene–ethyl acetate to afford **13** (1.17 g, 76%) as a syrup: $[\alpha]_D^{30}$ +5° (*c* 1.21, $CHCl_3$); PMR ($CDCl_3$) δ=0.98 (3H, d, 3-Me, J=7.0 Hz), 1.28 (3H, d, H-6, $J_{5,6}$=6.4 Hz), 1.7—2.5 (1H, m, H-3), 2.56 (2H, s, 4- and 5-OH), 3.24 (4H, s, S–CH_2–CH_2–S), 3.29 (1H, dd, H-4, $J_{3,4}$=8.2 Hz, $J_{4,5}$=3.0 Hz), 3.63 (1H, dd, H-2, $J_{1,2}$=9.0 Hz, $J_{2,3}$=1.9 Hz), 3.65 (3H, s, OMe), 3.93 (1H, dq, H-5), and 4.68 (1H, d, H-1). Found: C, 47.34; H, 7.76; S, 25.18%. Calcd for $C_{10}H_{20}O_3S_2$: C, 47.59; H, 7.99; S, 25.41%.

*4,5-Di-*O*-acetyl-3,6-dideoxy-3-*C*-methyl-2-*O*-methyl-D-galactose Ethylene Dithioacetal (14).* To a stirred ice-cooled solution of **13** (2.36 g, 9.35 mmol) in ethyl acetate (24 ml), acetic anhydride (2.12 ml, 22.5 mmol) and 4-dimethylaminopyridine (2.74 g, 22.5 mmol) were added successively; stirring was then continued at room temperature for 0.5 h. The resulting precipitates were filtered off and washed with ethyl acetate. The filtrate and washings were combined and washed successively with water, saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions, dried, and evaporated. The residual yellow syrup (3.25 g) was chromatographed on silica gel (100 g) with 6:1 benzene–ethyl acetate to afford a practically pure sample of **14** as colorless needles (2.88 g, 91.5%). Recrystallization from ethyl acetate–hexane gave a pure sample: mp 74.5—75.5 °C; $[\alpha]_D^{19}$ +30° (*c* 1.44, $CHCl_3$); PMR ($CDCl_3$) δ=0.90 (3H, d, 3-Me, J=7.0 Hz), 1.21 (3H, d, H-6, $J_{5,6}$=6.2 Hz), 2.10 and 2.18 (each 3H, each s, 4- and 5-OAc), 2.0—2.6 (1H, m, H-3), 3.18 (1H, dd, H-2, $J_{1,2}$=9.3 Hz, $J_{2,3}$=1.7 Hz), 3.23 (4H, s, S–CH_2–CH_2–S), 3.52 (3H, s, OMe), 4.62 (1H, d, H-1), 5.00 (1H, dd, H-4, $J_{3,4}$=8.2 Hz, $J_{4,5}$=3.2 Hz), and 5.18 (1H, dq, H-5). Found: C, 50.21; H, 7.16; S, 18.83%. Calcd for $C_{14}H_{24}O_5S_2$: C, 49.98; H, 7.19; S, 19.06%.

*4,5-Di-O-acetyl-3,6-dideoxy-3-C-methyl-2-O-methyl-D-galactose (**15**).* Red mercury(II) oxide (2.83 g, 13.1 mmol) and mercury(II) chloride (7.10 g, 26.2 mmol) were added successively at room temperature to a solution of **14** (2.00 g, 5.94 mmol) in aqueous 80% acetone (150 ml). The mixture was then stirred efficiently and refluxed under argon for 17 h. The resulting suspension was cooled and filtered through a super cell, and the filter cake was washed thoroughly with acetone. The filtrate and washings were combined and concentrated to remove the acetone. The aqueous residue was extracted with ethyl acetate, and the extract was washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The residual pale yellow syrup was chromatographed on silica gel (78 g) with 3:1 hexane–ethyl acetate to afford **15** as pale yellow plates (1.48 g, 95.4%): PMR ($CDCl_3$) δ=0.89 (3H, d, 3-Me, J=7.1 Hz), 1.20 (3H, d, H-6, $J_{5,6}$=6.1 Hz), 2.10 and 2.18 (each 3H, each s, 4- and 5-OAc), 2.1—2.7 (1H, m, H-3), 3.44 (3H, s, OMe), 3.3—3.6 (1H, m, H-2), 4.9—5.4 (2H, m, H-4 and H-5), and 9.75 (1H, d, H-1).

*5,6-Di-O-acetyl-2,4,7-trideoxy-4-C-methyl-1,3-di-O-methyl-D-galacto-1-enoheptitol (**16**).* A 4 M methylsulfinylmethanide anion in DMSO,[13a] prepared with sodium hydride (6.37 mmol as a 55% dispersion in mineral oil) and DMSO (1.7 ml), was added dropwise to a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (2.31 g, 6.73 mmol) in dry ether (35 ml) under argon at room temperature. The mixture was stirred for 10 min and then, to the resulting red suspension of the ylide, a solution of **15** (0.88 g, 3.37 mmol) in dry ether (18 ml) was added dropwise. After the mixture had been stirred at room temperature for 15 min, the resulting orange suspension was poured into ether (100 ml), and the organic layer was washed with water and a saturated aqueous NaCl solution, dried, and evaporated to a brown syrup (2.56 g). The syrup was chromatographed on silica gel (Mallinckrodt SILICAR CC-7 special, 80 g) with 4:1 hexane–ethyl acetate to afford a practically pure sample of **16** as a pale yellow syrup (0.70 g, 72%). A part of this sample was again chromatographed on the same silica gel with the same solvent system to give an analytically pure sample as a 7.7:1 mixture of the *E*- and *Z*-isomers: PMR ($CDCl_3$) δ=0.88 and 0.91 (3H, each d, 4-Me of *E*- and *Z*-isomers, J_E=7.3 Hz, J_Z=7.0 Hz), 1.19 (3H, d, H-7, $J_{6,7}$=6.7 Hz), 2.08 and 2.17 (each 3H, each s, 5- and 6-OAc), 3.16 and 3.18 (3H, each s, 1-OMe of *E*- and *Z*-isomers), 3.41 (1H, dd, H-3, $J_{2,3}$=9.0 Hz, $J_{3,4}$=3.0 Hz), 3.61 and 3.62 (3H, each s, 3-OMe of *E*- and *Z*-isomers), 6.10 and 6.48 (1H, each d, H-1 of *E*- and *Z*-isomers). Found: C, 58.30; H, 8.24%. Calcd for $C_{14}H_{24}O_6$: C, 58.31; H, 8.39%.

*5,6-Di-O-acetyl-2,4,7-trideoxy-4-C-methyl-3-O-methyl-D-galacto-heptose Dimethyl Acetal (**18**).* To an ice-cooled solution of **16** (1.05 g, 3.63 mmol) in methanol (10 ml) were added solid $NaHCO_3$ (0.37 g, 4.41 mmol) and NBS (0.77 g, 4.41 mmol) successively. After being stirred at 0 °C for 1 h, the mixture was evaporated and the residue was extracted with ethyl acetate. The extract was washed with water and a saturated aqueous NaCl solution, dried, and evaporated to afford a crystalline solid (1.60 g). Chromatography of the solid on silica gel (Mallinckrodt, 80 g) with 3:1 hexane–ethyl acetate gave colorless needles (1.08 g, 74.4%) as an epimeric mixture, **17**, of 5,6-di-*O*-acetyl-2-bromo-2,4,7-trideoxy-4-*C*-methyl-3-*O*-methyl-D-*glycero*-L-*manno*-heptose dimethyl acetal and its D-*glycero*-L-*gluco*-epimer. Tributylstannane (0.33 ml, 1.224 mmol) and α,α'-azobisisobutyronitrile (17 mg) were added to a solution of **17** (409 mg, 1.02 mmol) in dry benzene (6.1 ml). The solution was stirred, under an argon atmosphere, at 60 °C for 1 h and then evaporated. The residual syrup was chromatographed on silica gel (Mallinckrodt, 41 g) with 3:1 hexane–ethyl acetate to give **18** (315 mg, 96% based on **17**) as a syrup: PMR ($CDCl_3$) δ=0.85 (3H, d, 4-Me, J=7.0 Hz), 1.17 (3H, d, H-7, J=6.0 Hz), 2.07 and 2.14 (each 3H, each s, 5- and 6-OAc), 3.26 (3H, s, 3-OMe), 3.34 [6H, s, CH-$(OMe)_2$], 4.42 (1H, dd, H-1, $J_{1,2}$=5.0 Hz, $J_{1,2'}$=6.0 Hz), 4.98 (1H, dd, H-5, $J_{4,5}$=7.5 Hz, $J_{5,6}$=2.5 Hz), and 5.11 (1H, dq, H-6). Found: C, 56.29; H, 8.69%. Calcd for $C_{15}H_{28}O_7$: C, 56.23; H, 8.81%.

*Methyl 2,4,7-Trideoxy-4-C-methyl-3-O-methyl-β-D-galacto-heptopyranoside (**19**).* 1 M aqueous NaOH (9.86 ml) was added to an ice-cooled solution of **18** (1.58 g, 4.93 mmol) in dioxane (9.86 ml), after wihich the mixture was kept at room temperature for 2 h. The reaction mixture was neutralized (pH 7—8) with ion-exchange resin (CG 50 H^+ type), and the filtrate was evaporated to afford a crude syrup (1.21 g) of the deacetylation product. The pure sample of this product was obtained by column chromatography, using silica gel (Mallinckrodt) with 1:2 hexane–ethyl acetate as a colorless syrup, in an 87% yield (Found: C, 55.63; H, 9.84%. Calcd for $C_{11}H_{24}O_5$: C, 55.91; H, 10.24%). A solution of the crude syrup (1.21 g) in 0.5% methanolic hydrogen chloride (59 ml) was allowed to stand at room temperature for 1 h. The reaction mixture was then neutralized with solid $NaHCO_3$ and evaporated. The residue was extracted with ethyl acetate, and the extract was washed with a saturated aqueous NaCl solution, dried, and evaporated to give a pale yellow crystalline solid (1.19 g). The product was chromatographed on silica gel (59 g) with 5:1 chloroform–acetone to afford colorless needles (839 mg, 83% from **18**) melting at 88—98 °C. The PMR analysis (in $CDCl_3$) revealed that these crystals were a 1:5 mixture of α- and β-methyl glycoside, based on the areas of the signals at δ=4.35 (dd, $J_{1,2ax}$=9.8 Hz, $J_{1,2eq}$=2.2 Hz) and δ=4.94 (dd, $J_{1,2ax}$=4.0 Hz, $J_{1,2ex}$=1.5 Hz), which are attributed to the α- and β-anomeric protons respectively. The practically pure major β-anomer, **19**, was obtained on the recrystallization of the mixture from ethyl acetate–hexane as a first crop (366 mg, mp 99.5—101 °C) and a second crop (264 mg, mp 95—100.5 °C), the total yield from **18** being 62.4%. The pure sample of **19** was obtained by the recrystallization of the first crop from the same solvent system: mp 100—101 °C; $[\alpha]_D^{15}$ −102° (*c* 1.00, $CHCl_3$); PMR ($CDCl_3$) δ=0.99 (3H, d, 4-Me, J=6.5 Hz), 1.29 (3H, d, 6-Me, J=6.5 Hz), 1.2—1.7 (1H, m, H-2ax), 1.88 (1H, d, 6-OH), 1.4—2.0 (1H, m, H-4), 2.23 (1H, ddd, H-2eq, $J_{1,2eq}$=1.5 Hz, $J_{2eq,3}$=4.5 Hz, $J_{2eq,2ax}$=12.5 Hz), 3.0—3.6 (2H, m, H-3 and H-5), 3.35 and 3.37 (each 3H, each s, 1- and 3-OMe), 3.6—4.3 (1H, m, H-6), and 4.94 (1H, dd, H-1, $J_{1,2ax}$=4.0 Hz). Found: C, 58.99; H, 9.66%. Calcd for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87%.

*Methyl 2,4,7-Trideoxy-4-C-methyl-3-O-methyl-α-L-arabino-heptopyranosid-6-ulose (**20**)* A solution of **19** (0.24 g, 1.17 mmol) in acetone (4.8 ml) was cooled at −60 °C in a Dry Ice–acetone bath. After the addition of an aliquot (0.872 ml) of the Jones reagent prepared with CrO_3 (1.00 g), concd H_2SO_4 (0.861 ml), and water (2.88 ml), the mixture was allowed to warm to −10 °C and then stirred for 1.5 h; TLC analysis with 2:1 benzene–ethyl acetate then indicated the complete conversion of **19** into a single product, **20**. The reaction mixture was then neutralized with a saturated aqeuous $NaHCO_3$ solution and extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated to a pale yellow oil of crude **20** (0.23 g), which was subsequently chromatographed on silica gel

(8 g) with 5:1 benzene–ethyl acetate to afford a pure sample of **20** (0.22 g, 93%) as a colorless oil: $[\alpha]_D^{17}$ +4° (*c* 1.33, $CHCl_3$); IR (0.168 M, $CHCl_3$) 1720 cm^{-1}; PMR ($CDCl_3$) δ=0.95 (3H, d, 4-Me J=7.0 Hz), 1.53 (1H, ddd, H-2_{ax}, $J_{2ax,3}$=11.0 Hz, $J_{1,2ax}$=3.5 Hz, $J_{2ax,2eq}$=13.0 Hz), 2.22 (3H, s, H-7), 2.26 (1H, ddd, H-2eq, $J_{1,2eq}$=1.5 Hz, $J_{2eq,3}$=4.5 Hz), 3.27 (1H, ddd, H-3, $J_{3,4}$=9.5 Hz), 3.36 and 3.38 (each 3H, each s, 1- and 3-OMe), 3.77 (1H, d, H-5, $J_{4,5}$=10.5 Hz), and 4.96 (1H, dd, H-1). Found: C, 59.41; H, 8.76%. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97%.

*Hydrazone **21** of **20**.* A mixture of **20** (0.20 g, 8.35 mmol), ethanol (2 ml), triethylamine (1.17 ml, 8.35 mmol), and 100% hydrazone hydrate (0.191 ml, 3.93 mmol) was refluxed for 1 h. After cooling, the reaction mixture was neutralized with carbon dioxide gas and extracted with chloroform (30 ml). The extract was washed with water, and the aqueous layer was again extracted with chloroform. The combined chloroform layers were washed with a saturated aqueous NaCl solution, dried, and evaporated to afford practically pure colorless needles of **21** (0.21 g, 98%). Recrystallization from chloroform–petroleum ether gave a pure sample: mp 71—72 °C; $[\alpha]_D^{18}$ −72° (*c* 1.11, $CHCl_3$); IR (KBr) 3400 (NH_2) and 1630 cm^{-1} (C=N). Found: C, 55.44; H, 9.20; N, 12.97%. Calcd for $C_{10}H_{20}N_2O_3$: C, 55.53; H, 9.32; N, 12.95%.

*Methyl 2,4,6,7-Tetradeoxy-6-iodo-4-*C*-methyl-3-*O*-methyl-α-*L*-arabino-hept-6-enopyranoside (**22**).* The hydrazone **21** (0.20 g, 0.929 mmol) in THF (9.1 ml) and triethylamine (6.48 ml) was treated with iodine (0.52 g, 2.05 mmol) in THF (1.0 ml) at room temperature with stirring under argon. Initially the iodine color was discharged, triethylamine hydroiodide being precipitated and gas evolved. The orange-colored suspension was stirred at room temperature for 45 min and then diluted with chloroform (75 ml). The mixture was washed with water, 2 M hydrochloric acid, a 5% aqueous $Na_2S_2O_3$ solution (30 ml), and a saturated aqueous NaCl solution, dried, and evaporated. The residual dark brown syrup (0.34 g) was chromatographed on silica gel (13 g) with 15:1 benzene–ethyl acetate to afford colorless needles of **22** (0.21 g, 72%). Recrystallization from ethyl acetate–hexane gave an analytical sample: mp 86—87 °C; $[\alpha]_D^{20}$ −74° (*c* 1.06, $CHCl_3$); IR (0.15 M, $CHCl_3$) 1620 cm^{-1} (C=C); PMR ($CDCl_3$) δ=0.88 (3H, d, 4-Me, J=7.0 Hz), 1.2—1.9 (1H, m, H-4), 1.51 (1H, ddd, H-2ax, $J_{1,2ax}$=3.5 Hz, $J_{2ax,3}$=11.5 Hz, $J_{2ax,2eq}$=13.0 Hz), 2.25 (1H, ddd, H-2eq, $J_{1,2eq}$=1.5 Hz, $J_{2eq,3}$=11.5 Hz), 3.23 (1H, d, with a little long range coupling with H-7′, H-5, $J_{4,5}$=10.0 Hz), 3.1—3.7 (1H, m, H-3), 3.39 (6H, s, 1- and 3-OMe), 4.94 (1H, dd, H-1), 6.01 (1H, d, H-7 or H-7′, $J_{7,7'}$=1.2 Hz), and 6.40 (1H, m, H-7′ or H-7). Found: C, 38.28; H, 5.38; I, 40.32%. Calcd for $C_{10}H_{17}O_3I$: C, 38.48; H, 5.49; I, 40.65%.

*Condensation of **22** with Benzaldehyde* via *the Lithium Compound, **23**.* A solution of **22** (30.4 mg, 0.097 mmol) in dry ether (0.25 ml) was cooled to −78 °C. To the resulting white suspension was added a 1.6 M butyllithium in hexane (0.0729 ml, 0.117 mmol) using a syringe. After the resulting pale yellow solution had been stirred at −78 °C for 2.5 h, benzaldehyde (0.0119 ml, 0.117 mmol) was added slowly *via* the syringe to the solution of the alkenyllithium, **23**, thus formed; stirring was then continued for 1.5 h. The reaction mixture was quenched at 0 °C by the addition of an aqueous saturated NH_4Cl solution, and was then extracted with ether. The organic layers were washed with a saturated aqueous NaCl solution, dried, and evaporated to a pale yellow oil (62.7 mg). The crude product was purified by chromatography on silica gel (3.1 g) with 5:1 hexane–acetone to afford a colorless syrup (15.4 mg, 54%) of the condensation product, **24**, as a 1:1.2 mixture of epimers: PMR ($CDCl_3$) δ=0.78 and 0.84 (3H, each d, 4-Me, J=7.0 Hz), 1.1—1.9 (2H, m, H-2ax H-4), 2.0—2.5 (1H, m, H-2eq), 2.7—2.9 (1H, br, OH), 2.9—3.5 (1H, m, H-3), 3.24, 3.26, 3.35, and 3.39 (6H, each s, 1- and 3-OMe), 3.93 (1H, dd, H-5, $J_{4,5}$=10.5 Hz, $J_{5,=CH}$=2.5 Hz), 4.91 (1H, dd, H-1, $J_{1,2eq}$=1.5 Hz, $J_{1,2ax}$=3.5 Hz), 5.1—5.5 (3H, m, =CH and benzylic H), and 7.42 (5H, s, ArH); M^+ 292 (20 eV).

*Methyl 2,4,6,7-Tetradeoxy-4-*C*-methyl-3-*O*-methyl-α-*D*-arabino-hept-6-enopyranoside (**25**).* The iodide, **22** (0.185 g), was added to a solution of KOH (0.66 g) in ethanol (6.5 ml), after which the mixture was refluxed with stirring for 1.5 h. After cooling, the mixture was neutralized with carbon dioxide gas and extracted with ether (30 ml). The ethereal extract was washed with water and a saturated aqueous NaCl solution, and dried. After the removal of the solvent, the residual brown oil (0.128 g) was chromatographed on silica gel (7 g) with 20:1 benzene–ethyl acetate to afford a colorless oil of **25** (80 mg, 74%): $[\alpha]_D^{19}$ −80° (*c* 0.84, $CHCl_3$; IR (0.211 M, $CHCl_3$) 3300 cm^{-1} (≡CH); PMR ($CDCl_3$) δ=1.10 (3H, d, 4-Me, J=7.0 Hz), 1.49 (1H, ddd, H-2ax, $J_{1,2ax}$=3.5 Hz, $J_{2ax,3}$=11.5 Hz, $J_{2ax,2eq}$=13.0 Hz), 1.3—2.1 (1H, m, H-4), 2.21 (1H, ddd, H-2eq, $J_{1,2ex}$=1.5 Hz, $J_{2eq,3}$=4.5 Hz), 2.45 (1H, d, H-7, $J_{5,7}$=2.5 Hz), 3.22 (1H, ddd, H-3, $J_{3,4}$=9.8 Hz), 3.36 and 3.39 (each 3H, each s, 1- and 3-OMe), 4.14 (1H, dd, H-5, $J_{4,5}$=10.5 Hz), and 4.90 (1H, dd, H-1). Found: C, 65.16; H, 8.57%. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%.

*Methyl 2,4,6,7-Tetradeoxy-7-iodo-4,6-di-*C*-methyl-3-*O*-methyl-α-*L*-arabino-hept-6-enopyranoside (**27**).* A solution of dimethyl sulfide complex[18] of copper(I) bromide (86.6 mg, 0.42 mmol) in ether (0.5 ml) and dimethyl sulfide (0.4 ml) under argon was cooled to −45 °C, at which temperature a white solid was formed; 1.71 M methylmagnesium bromide in ether (0.246 ml, 0.42 mmol) was then added dropwise using a syringe over a period of 2 min. The resulting suspension of a yellow solid was stirred at −45 °C for 2 h, after which a solution of **25** (64.7 mg, 0.351 mmol) in ether (0.15 ml) was added and the mixture was stirred at −25 °C for 1 week. The resulting dark green reaction mixture was cooled to −50 °C, and to this stirred mixture was added iodine (0.107 g, 0.42 mmol). After the mixture had been stirred at −30 °C for 2 h, to the red-brown reaction mixture was added triethyl phosphite (0.024 ml) and 5 M hydrochloric acid (0.524 ml) at the same temperature. The resulting mixture was diluted with ether (20 ml), washed with saturated aqueous $NaHCO_3$ and NaCl solutions, and evaporated after being dried. The residue was chromatographed on silica gel (5.8 g) with 20:1 hexane–acetone to afford **27** (59.6 mg, 52%) as colorless needles and **25** (12.2 mg, 18.9%). A pure sample of **27** was obtained by recrystallization from ethyl acetate and hexane: mp 84—85 °C; $[\alpha]_D^{16}$ −75° (*c* 1.11, $CHCl_3$); IR (KBr) ν_{max}=1620 cm^{-1} (C=C); PMR ($CDCl_3$) δ=0.83 (3H, d, 4-Me, J=7.0 Hz), 1.2—1.8 (1H, m, H-4), 1.49 (1H, ddd, H-2ax, $J_{1,2ax}$=3.5 Hz, $J_{2ax,3}$=11.5 Hz, $J_{2ax,2eq}$=13.0 Hz), 1.86 (3H, d, 6-Me, J=1.2 Hz), 2.26 (1H, ddd, H-2eq, $J_{1,2ex}$=1.5 Hz, $J_{2eq,3}$=4.5 Hz), 2.9—3.5 (1H, m, H-3), 3.36 and 3.39 (each 3H, each s, 1- and 3-OMe), 3.94 (1H, d, H-5, $J_{4,5}$=10.5 Hz), 4.89 (1H, dd, H-1), and 6.34 (1H, m, H-7). Found: C, 40.68; H, 5.93; I, 38.62%. Calcd for $C_{11}H_{19}O_3I$: C, 40.51; H, 5.87; I, 38.91%.

*Reaction of Ethylene Oxide with Complexed Organocopper Reagent **26*** via *Mixed Cuprate.* By the same procedure as was used in the preparation of **27**, a dark green solution of the alkenylcopper intermediate **26** was prepared from **25** (47.4

mg, 0.257 mmol) and cooled to −78 °C. A solution of 1-lithiopentyne prepared from butyllithium (0.308 mmol) and 1-pentyne (0.308 mmol) in ether (0.37 ml), to which HMPA (0.108 ml, 0.616 mmol) had been added, was transferred to the solution of **26** mentioned above. After being stirred for 1 h, ethylene oxide (0.0153 ml, 0.308 mmol) was slowly added with a chilled syringe. The resulting mixture was stirred at −78 °C for 2.5 h, allowed to stand at −25 °C for 24 h, and worked up by the procedure described by McGuirk *et al.*[24] The resulting yellow-green oil (66.4 mg) was chromatographed on silica gel (3.5 g) with 10:1 hexane–acetone to afford a pale yellow syrup (29.2 mg, 46.5%) of the homoallylic alcohol **28**: PMR ($CDCl_3$) δ=0.84 (3H, d, 4-Me, J=7.0 Hz), 1.1—1.9 (2H, m, H-2ax and H-4), 1.69 (3H, d, 6-Me, J=1.0 Hz), 1.79 (1H, br, 9-OH), 2.0—2.6 (3H, m, H-2eq, H-8 and 8′), 3.0—3.5 (1H, m, H-3), 3.35 and 3.39 (each 3H, each s, 1- and 3-OMe), 3.5—3.9 (2H, m, H-9, 9′), 3.75 (1H, d, H-5, $J_{4,5}$=9.5 Hz), 4.88 (1H, dd, H-1, $J_{1,2eq}$=1.5 Hz, $J_{1,2ax}$=3.5 Hz), and 5.46 (1H, m, H-7). Further purification of this sample by repeated chromatography failed to give an analytically pure sample of **28**, but the acetylation of the sample with acetic anhydride in pyridine afforded the pure acetate of **28** showing *m/e* 287 (M^++1) and 286 (M^+) in its mass spectrum: PMR ($CDCl_3$) δ=0.83 (3H, d, 4-Me, J=7.0 Hz), 1.2—1.7 (1H, m, H-4), 1.46 (1H, ddd, H-2ax, $J_{1,2ax}$=3.5 Hz, $J_{2ax,3}$=9.0 Hz, $J_{2ax,2eq}$=13.0 Hz), 1.65 (3H, d, 6-Me, $J_{6\text{-Me},7}$=1.2 Hz), 2.02 (3H, s, OAc), 2.25 (1H, ddd, H-2eq, $J_{1,2eq}$=1.5 Hz, $J_{2eq,3}$=4.5 Hz), 2.42 (2H, dt, H-8, 8′, $J_{7,8}$=6.8 Hz, $J_{8,9}$=7.2 Hz), 3.0—3.4 (1H, m, H-3), 3.32 and 3.36 (each 3H, each s, 1- and 3-OMe), 3.72 (1H, d, H-5, $J_{4,5}$=10.5 Hz), 4.09 (2H, t, H-9, 9′), 4.88 (1H, dd, H-1), and 5.41 (1H, m, H-7).

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