June, 1981] © *1981 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, *54*, *1743—1748 (1981)* 1743

# Synthetic Studies of Rifamycins. III.[1] The Partial Synthesis of Rifamycin Ansa-chain Compounds from Their Degradation Products†

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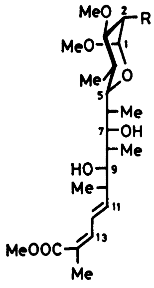
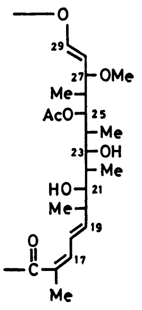
The ansa-chain compound methyl [methyl 2,4,6,8,10,11,12,13,14-nonadeoxy-4,6,8,10,14-penta-*C*-methyl-3-*O*-methyl-L-*manno*-β-D-*galacto*-(11*E*,13*Z*)-11,13-pentadecadienopyranosid]uronate (**1a**) and its (*R*)-2-bromo derivative, **1b**, were transformed into the corresponding 7,9-diacetate **3a** and **3b** or the 7,9-acetonide **7a** and **7b**. The ozonolysis of **3a** or **3b** gave methyl 7,9-di-*O*-acetyl-2,4,6,8,10-pentadeoxy-4,6,8,10-tetra-*C*-methyl-3-*O*-methyl-L-*manno*-β-D-*galacto*-undecodialdopyranoside-(1,5) (**4a**) or its (*R*)-2-bromo derivative (**4b**) respectively. The Wittig condensation of **4b** with (methoxycarbonylmethylene)triphenylphosphorane, followed by debromination with tributylstannane, afforded 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 (**6a**). The diisobutylaluminium hydride reduction of **6a**, followed by acetonation, gave methyl 2,4,6,8,10,11,12-heptadeoxy-7,9-*O*-isopropylidene-4,6,8,10-tetra-*C*-methyl-3-*O*-methyl-L-*manno*-β-D-*galacto*-(*E*)-11-tridecenopyranoside-(1,5) (**10a**). The allylic alcohol, **10a**, was converted into the allylic bromide, **12a**, which then yielded the triphenylphosphonium bromide, **13a**. The Wittig condensation of the reactive ylide generated from **13a** with methyl pyruvate afforded a 4 : 5 mixture of **7a** and its 13*E*-isomer. The partial synthesis of **1a** was accomplished by the selective hydrolysis of the **7a** isolated from the mixture.

The ansa-chain compound **1a**,[2] corresponding to the 25-deacetylated ansa-bridge portion, **2**, of rifamycin B, O, S, and SV, has recently been obtained *via* its (*R*)-2-bromo derivative, **1b**, itself produced by the novel degradation of 25-deacetylrifampicin. During the course of our studies of the synthesis of **1a**,[1] a degradation-reconstruction program of **1a** and **1b** has been undertaken to secure materials for establishing the structure of the synthetic intermediate, **4a** or **6a**, and to survey the practical methods for the construction of **1a** starting with **4a** or **6a**. This paper will describe the partial degradation of **1a** or **1b** to their synthetic intermediates, **4a**, **4b**, **8a**, and **8b**, and the partial synthesis of **1a** or **1b** from the degradation products *via* the intermediates, **6a**, **9a** or **9b**, and **10a** or **10b**, by Wittig reaction.



1a R=H
1b R=Br



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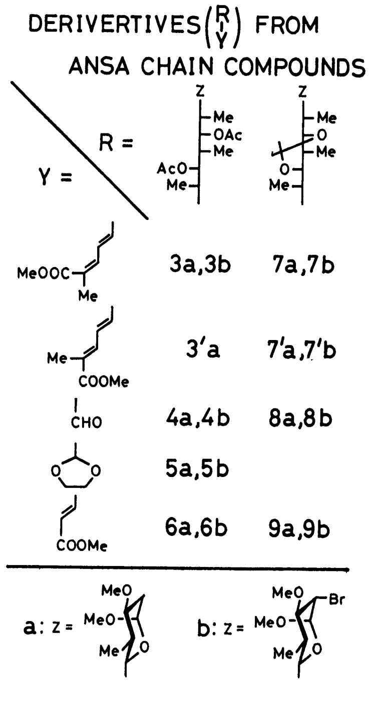
The acetylation of **1a** with acetic anhydride in pyridine afforded a mixture of the diacetate, **3a** (15%), and its 13*E*-isomer, **3′a** (22%), and a mixture of the monoacetate of **1a** (20%) and its 13*E*-isomer (18%). The structures of the isomeric products were confirmed by the $^1$H-NMR data. On the contrary, the acetylation of **1b** with acetic anhydride and 4-dimethylaminopyridine (DMAP) in ethyl acetate gave the diacetate, **3b**, as the sole product in a 90% yield.[3] Both **1a** and **1b** were smoothly acetonated with 2,2-dimethoxypropane (DMP) in acetone containing a small amount of sulfuric acid to afford the 7,9-acetonides, **7a** and **7b**, in 99% and 76% yields respectively. Although it is unclear why the bromine atom situated far from the unsaturated system of the molecule of **1b** prevents its 13 *Z*-geometry from geometrical isomerization during acetylation, the unsaturated system of a free ansa-chain compound such as **1a** seems to be less stable than that of the intact ansa-chain in rifamycins.



The ozonolysis of a mixture of **3a** and **3′a** with ozone and dimethyl sulfide in dichloromethane[4] gave the aldehyde, **4a**, in a 77% yield: this is a strategic intermediate in the synthesis of **1a**. The direct treatment of **4a** with ethylene glycol and *p*-toluenesulfonic acid in

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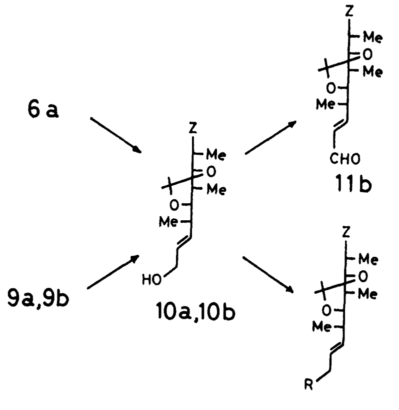
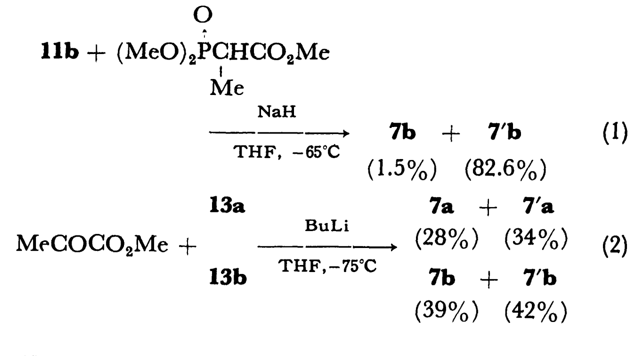
acetonitrile failed, however, to afford the ethylene acetal, **5a**, because of the simultaneous hydrolysis of the cyclic methyl acetal moiety of **4a**, and so the following alternative process was necessary. The ozonolysis of **3b**, followed by the treatment of the resulting aldehyde, **4b**, with ethylene glycol, gave the crystalline ethylene acetal, **5b**, in a 53% yield; on selective hydrolysis with 70% trifluoroacetic acid (TFA), this then provided **4b** in a quantitative yield. The debromination of **5b** with tributylstannane afforded plates of **5a** in a 64% yield after recrystallization. Attempts to obtain **4a** by the selective hydrolysis of the ethylene acetal group of **5a** were all unsuccessful. From these results, it was found that **5a** was not a synthetic precursor suitable for **4a**, while **5b** was a useful precursor for **4b**. The useful derivative, **6a**,[5] was obtained in a 95% yield by the debromination of **6b**, which had itself prepared by the Wittig condensation of **4b** with (methoxycarbonylmethylene)triphenylphosphorane in an 84% yield. The ozonolysis of **7a** or **7b**, followed by the Wittig condensation of the resulting aldehyde, **8a** or **8b** with the phosphorane, gave **9a** or **9b** in an 88 or 70% yield respectively.

We examined the possibility of the formation of **7a** *via* the allylic alcohol, **10a**, from **6a** or **9a**. At the same time, the transformation of **9b** into **7b** *via* **10b** was also examined, taking into account the fact that **7b** might be more stable than **7a** in the geometrical isomerization of an unsaturated system. The treatment of **6a** with diisobutylaluminium hydride (DIBAL) in toluene led to the corresponding triol, which, without purification, was acetonated with DMP in DMF containing *p*-toluenesulfonic acid to afford **10a** in a 73% yield. The reduction of **9a** or **9b** with DIBAL in toluene gave **10a** or **10b** in a 70 or 96% yield respectively. At first, the condensation of the phosphonate anion generated from dimethyl [1-(methoxycarbonyl)ethyl]phosphonate (**14**) with the α,β-unsaturated aldehyde, **11b**, which had been obtained in a 62% yield by the oxidation of **10b** with chromium trioxide in hexamethylphosphoric triamide (HMPA),[6] was examined. The reaction was carried out in THF at −75—−60 °C to afford, predominantly, the undesired 11*E*,13*E*-isomer **7'b** in an 83% yield, accompanied by a small amount of **7b** (1.5%) [Reaction 1]. The structure of **7'b** was confirmed by the $^1$H-NMR data. This reaction was highly stereoselective, and similar results have been reported in a recent paper;[7] therefore, it was conclusively disadvantageous for the formation of the desired 11*E*,13*Z*-isomer **7b**.



12a,12b: R=Br
13a,13b: R=PPh$_3$Br



$$\mathbf{11b} + (\mathrm{MeO})_2\overset{\overset{\large O}{\vdots}}{\mathrm{P}}\underset{\underset{\large Me}{|}}{\mathrm{C}}\mathrm{HCO_2Me} \xrightarrow[\text{THF, }-65\,^\circ\mathrm{C}]{\text{NaH}} \underset{(1.5\%)}{\mathbf{7b}} + \underset{(82.6\%)}{\mathbf{7'b}} \qquad (1)$$

$$\mathrm{MeCOCO_2Me} + \begin{matrix}\mathbf{13a}\\ \\ \mathbf{13b}\end{matrix} \xrightarrow[\text{THF, }-75\,^\circ\mathrm{C}]{\text{BuLi}} \begin{matrix}\underset{(28\%)}{\mathbf{7a}} + \underset{(34\%)}{\mathbf{7'a}}\\ \underset{(39\%)}{\mathbf{7b}} + \underset{(42\%)}{\mathbf{7'b}}\end{matrix} \qquad (2)$$

House and Rasmusson[8] reported that the Wittig condensation of [1-(methoxycarbonyl)ethylidene]triphenylphosphorane with acetaldehyde gave a 27.6 : 1 mixture of methyl tiglate and methyl angelate, while the reaction of ethylidenetriphenylphosphorane and methyl pyruvate provided a 2.13 : 1 mixture of tiglate and angelate. As the second approach to **7a** or **7b**, we condensed methyl pyruvate with the reactive ylide formed from a triphenylphosphonium salt, such as **13a** or **13b**. The allylic alcohol, **10a** or **10b**, was then transformed into the corresponding allylic bromide, **12a** (79%) or **12b** (90%), by treatment with mesyl chloride and a mixture of triethylamine, lithium bromide, and dichloromethane.[9] The reaction of **12a** or **12b** with triphenylphosphine in benzene afforded **13a** or **13b** in a quantitative yield. The phosphonium bromide, **13a** or **13b**, was treated with butyllithium in THF at −75 °C and then allowed to react with methyl pyruvate at the same temperature to give a 4 : 5 mixture of **7a** and **7'a** or an 1 : 1 mixture of **7b** and **7'b** in a 62 or 81% yield respectively (Reaction 2). The desired condensation product, **7a** (28%) or **7b** (39%), was separated from the isomer, **7'a** or **7'b**, by alumina-column chromatography or by preparative layer chromatography (PLC) on silica gel, which was identical with the aforesaid corresponding sample. The structure of isomeric product, **7'a**, was confirmed by the $^1$H-NMR data.

A recent publication[10] described a new stereospecific process for the conversion of an aldehyde to a 5-substituted (2*Z*,4*E*)-2-methyl-2,4-pentadienoic acid *via* the lactone of 5-substituted 5-hydroxy-2-methyl-2-pentenoic acid. This reaction process, reported after our work had been completed, is undoubtedly better than our five-step process starting with **4a**, provided that the new process is applicable to **4a** for the synthesis of **1a**. Although Reaction 2 seems to be almost non-stereoselective, it is noteworthy that the reaction yielded a significant amount of (*Z*)-olefins compared with Reaction 1. Furthermore, when the Wittig reaction (2) is carried out by an intramolecular version[11] for the purpose of the construction of the medium ring of unsaturated lactone or the macrocyclic lactam ring of rifamycins, it may be expected that the tendency to form the desired (*Z*)-olefin is strengthened, because the formation of the intermediate betaine with the erythro configuration,[12] the precursor of (*Z*)-olefin, might be kinetically more favored in the intramolecular cyclization of the lactone or the lactam than in the intermolecular reaction.

The last step of the synthesis of **1a** was the selective deacetonation of **7a**, which was effected with 50% difluoroacetic acid (DFA) at 0 °C to afford **1a** in an 80% yield. The treatment of **7b** with 90% TFA at 0 °C gave **1b**, which could then be converted into **1a** by debromination.[2)]

## 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 $^1$H-NMR spectra were determined in $CDCl_3$ with either a Varian A60 or EM-390 spectrometer, using TMS as the internal standard. The TLC was performed on Merck TLC plates, 60F-254 0.25 mm. The PLC was carried out on precoated PLC plates (20×20×0.5 mm) of Merck Kieselgel 60F-254. The column chromatography was performed on silica gel, Wakogel C-200. In general, evaporation was conducted under reduced pressure below 30 °C.

*Methyl [Methyl 7,9-Di-*O*-acetyl-2,4,6,8,10,11,12,13,14-nona-deoxy-4,6,8,10,14-penta-*C*-methyl-3-*O*-methyl-*L-manno-β-D-galacto*(11*E*, 13*Z*)-11,13-pentadecadienopyranosid]uronate (3a) and 13*E*-Isomer (3′a).*  A mixture of **1a** (253 mg, 0.590 mmol), acetic anhydride (1.35 ml, 14.3 mmol), and dry pyridine (2.5 ml) was allowed to stand at 40 °C for 6 d. The mixture was then poured into ice water and extracted with ether. The ether layer was washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (30 g) with 10: 1 benzene–acetone to afford the following four fractions: **3a**, 45 mg (15%); $R_f$ 0.37 (8: 1 benzene–acetone); mp 132—133 °C (ether); $[\alpha]_D^{29}$ +30° (*c* 1.0, MeOH); UV$_{max}$ (EtOH) 262 nm (ε 23100); IR (KBr) 1732, 1710, 1641, and 1607 cm$^{-1}$; $^1$H-NMR δ=0.8—1.1 (12H, m, 4, 6, 8, and 10-Me), 1.94 (6H, broad s, 14-Me and OAc), 2.01 (3H, s, OAc), 3.32 and 3.34 (each 3H, each s, OMe×2), 3.76 (3H, s, COOMe), 4.7—5.2 (3H, m, H-1,7, and 9),5.68 (1H, dd, H-11, $J_{10,11}$= 8.9 Hz, $J_{11,12}$=15.0 Hz), 6.32 (1H, m, H-13, $J_{12,13}$=11.0 Hz, $J_{13,Me}$=1.9 Hz), and 7.08 (1H, dd, H-12) [Found: C, 63.16; H, 8.52%. Calcd for $C_{27}H_{44}O_9$: C, 63.26; H, 8.65%]; **3′a**, 68 mg (22%); $R_f$ 0.33; mp 146—147 °C (acetone); $[\alpha]_D^{31}$ −33° (*c* 0.9, MeOH); UV$_{max}$ (EtOH) 263 nm (ε 26600); IR (KBr) 1732, 1703, and 1641 cm$^{-1}$; $^1$H-NMR δ=0.8—1.1 (12H, m, 4, 6, 8, and 10-Me), 1.94 (6H, broad s, 14-Me and OAc), 2.01 (3H, s, OAc), 3.32 and 3.34 (each 3H, each s, OMe×2), 3.73 (3H, s, COOMe), 4.7—5.2 (3H, m, H-1,7, and 9), 5.91 (1H, dd, H-11, $J_{10,11}$=8.2 Hz, $J_{11,12}$=14.8 Hz), 6.34(1H, dd, H-12, $J_{12,13}$=10.4 Hz), and 7.10 (1H, m, H-13, $J_{13,Me}$=1.5 Hz) [Found: C, 63.08; H, 8.44%. Calcd for $C_{27}H_{44}O_9$: C, 63.26; H, 8.65%]; monoacetate of **1a**, 54 mg (20%); $R_f$ 0.24; $^1$H-NMR δ=1.96 (3H, s, 7 or 9-OAc), 5.74 (1H, dd, H-11, $J_{11,12}$=15 Hz, $J_{10,11}$=9.0 Hz), 6.34 (1H, dd, H-13, $J_{12,13}$=11.0 Hz), and 7.09 (1H, dd, H-12), and mono-acetate of 13*E*-isomer of **1a**, 49 mg (18%); $R_f$ 0.21; $^1$H-NMR δ=1.96 (3H, s, 7 or 9-OAc), 5.91 (1H, dd, H-11, $J_{11,12}$= 14.7 Hz, $J_{10,11}$=8.0 Hz), 6.34 (1H, dd, H-12, $J_{12,13}$=10.0 Hz), and 7.11 (1H, dd, H-13, $J_{13,Me}$=1.0 Hz).

*(*R*)-2-Bromo Deivative (3b).*  A mixture of **1b** (199 mg, 0.393 mmol), acetic anhydride (0.371 ml, 3.93 mmol), DMAP (106 mg, 0.864 mmol), and ethyl acetate (2 ml) was stirred at 45 °C for 24 h. The mixture was then diluted with ethyl acetate (18 ml) and washed with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions successively, dried, and evaporated. The residual brown syrup (270 mg) was chromatographed on silica gel (23 g) with 8: 1 benzene–ethyl acetate to afford **3b** (210 mg, 90%) as a colorless syrup: $[\alpha]_D^{29}$ +16° (*c* 0.77, MeOH); UV$_{max}$ (EtOH) 264 nm (ε 21300); IR ($CCl_4$) 1737, 1641, and 1605 cm$^{-1}$, $^1$H-NMR δ=0.88—1.08 (12H, m, 4, 6, 8, and 10-Me), 1.93 (6H, s, 14-Me and OAc), 2.00 (3H, s, OAc), 3.16 (1H, dd, H-3, $J_{2,3}$=3.0 Hz, $J_{3,4}$=10.0 Hz), 3.35 (6H, s, OMe×2), 3.74 (3H, s, COOMe), 4.28 (1H, dd, H-2, $J_{1,2}$=1.5 Hz), 4.8—5.1 (3H, m, H-1,7, and 9), 5.64 (1H, dd, H-11, $J_{10,11}$=9.0 Hz, $J_{11,12}$=15.1 Hz), 6.30 (1H, m, H-13, $J_{12,13}$=10.7 Hz, $J_{13,Me}$=1 Hz), and 7.07 (1H, dd, H-12).

Found: C, 54.53; H, 7.18; Br, 13.27%. Calcd for $C_{27}H_{43}O_9Br$: C, 54.82; H, 7.33; Br, 13.51%.

*Methyl 7,9-Di-*O*-acetyl-2,4,6,8,10-pentadeoxy-4,6,8,10-tetra-*C*-methyl-3-*O*-methyl-*L-manno-β-D-galacto*-undecodialdopyranoside-(1,5) (4a).*  A mixture of **3a** and **3′a** (74 mg, 0.144 mmol) was dissolved in dry dichloromethane (3.68 ml), and then the mixture was cooled to −75 °C. Ozonolyzed oxygen gas (475 ml) containing 0.287 mmol of ozone was passed through the solution at the rate of 23.8 ml/min. To the resulting solution was added dimethyl sulfide (0.105 ml, 1.44 mmol) at the same temperature. The mixture was gradually warmed to room temperature over the period of 3 h and then washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup was chromatographed on silica gel (3 g) with 8: 1 benzene–acetone to give **4a** (46 mg, 77%) as a pale yellow syrup: $^1$H-NMR δ=0.85—1.15 (12H, m, 4,6,8, and 10-Me), 2.02 and 2.04 (each 3H, oach s, OAc×2), 3.32 and 3.37 (each 3H, each s, OMe×2), 4.8—5.5 (3H, m, H-1,7, and 9), and 9.50 (1H, d, H-11, $J_{10,11}$=3.3 Hz).

*(*R*)-2-Bromo Derivative (4b) and Its 11-Ethylene Acetal (5b).* A sample (163 mg) of **3b** was ozonolyzed by the procedure described in the preparation of **4a** and then worked-up to afford the crude aldehyde, **4b**, as a syrup. A mixture of the crude **4b** (137 mg), ethylene glycol (0.153 ml), anhydrous *p*-toluenesulfonic acid (4.8 mg), and dry acetonitrile (1.4 ml) was stirred at room temperature for 0.5 h. The reaction mixture was then poured into ice-cooled water containing $NaHCO_3$ (2.3 mg) and extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (218 mg) was chromatographed on silica gel (20 g) with 4 : 1 benzene–ethyl acetate to give **5b** (78 mg, 53%) as a colorless solid. Recrystallization from 1 : 1 acetone–hexane afforded needles of **5b**: mp 142—143 °C; $[\alpha]_D^{30}$ −47° (*c* 0.96, MeOH); IR (KBr) 1737 cm$^{-1}$; $^1$H-NMR δ=0.92, 0.95, 0.98, and 1.00 (each 3H, each d, 4,6,8, and 10-Me, *J*=7 Hz), 2.02 (6H, s, OAc×2), 3.17 (1H, dd, H-3, $J_{2,3}$=3.5 Hz, $J_{3,4}$=9.9 Hz), 3.37 (6H, s, OMe×2), 3.7—4.0 (4H, m, $-OCH_2CH_2O-$), 4.35 (1H, dd, H-2, $J_{1,2}$=1.6 Hz), 4.73 (1H, d, H-11, $J_{10,11}$=3.4 Hz), 4.92 (1H, d, H-1), and 5.0—5.4 (2H, m, H-7 and 9).

Found: C, 51.30; H, 7.16; Br, 14.71%. Calcd for $C_{23}H_{39}O_9Br$: C, 51.21; H, 7.29; Br, 14.81%.

A sample (65 mg) of **5b** was dissolved in 70 (v/v)% aqueous TFA (0.65 ml) and allowed to stand at 0—2 °C for 20 h. The reaction mixture was then poured into cold chloroform and neutralized with solid $NaHCO_3$. The organic layer thus separated was washed with water and a saturated aqueous NaCl solution, dried, and evaproated to give a practically pure sample of **4b** (60 mg, 100%); $^1$H-NMR δ=0.94, 0.99, 1.02, and 1.10 (each 3H, each d, 4,6,8, and 10-Me, *J*=6.5 and 7.0 Hz), 2.01 and 2.03 (each 3H, each s, OAc×2), 3.17 (1H, dd, H-3, $J_{2,3}$=3.4 Hz, $J_{3,4}$=10.1 Hz), 3.37 (6H, s, OMe×2), 4.34 (1H, dd, H-2, $J_{1,2}$=1.5 Hz), 4.91 (1H, d, H-1), 4.9—5.2 (1H, m, H-7 or H-9), 5.39 (1H, dd, H-7 or

H-9, $J$=2.0 and 9.4 Hz), and 9.56 (1H, d, H-11, $J_{10,11}$=3.2 Hz).

*11-Ethylene Acetal (5a).* To a solution of **5b** (81 mg, 0.150 mmol) in dry benzene (2.0 ml) was added tributylstannane (0.048 ml, 0.180 mmol) and α,α′-azobisisobutyronitrile (AIBN) (4.9 mg, 0.03 mmol). The mixture was then stirred at 60 °C for 6 h under argon. The reaction mixture was evaporated, and the residue (198 mg) was chromatographed on silica gel (10 g) with 3: 1 benzene–ethyl acetate to afford **5a** (44 mg, 64%) as a colorless solid. Recrystallization from 1 : 2 acetone–hexane gave colorless plates: mp 113—114 °C; $[\alpha]_D^{20}$ −85° (*c* 1.0, MeOH); IR (KBr) 1731 cm$^{-1}$; $^1$H-NMR δ=0.86−1.08 (12H, m, 4, 6, 8, and 10-Me), 1.2—1.7 (1H, m, H-2ax), 2.05 (6H, s, OAc×2), 3.35 and 3.37 (each 3H, each s, OMe×2), 3.8—4.0 (4H, m, $-OCH_2CH_2O-$), 4.76 (1H, d, H-11, $J_{10,11}$=3.5 Hz), and 4.7—5.4 (3H, m, H-1,7, and 9).

Found: C, 59.74; H, 8.57%. Calcd for $C_{23}H_{40}O_9$: C, 59.98; H, 8.75%.

*Methyl [Methyl 7,9-Di-O-acetyl-2-bromo-2, 4, 6, 8, 10, 11, 12-heptadeoxy-4, 6, 8, 10-tetra-C-methyl-3-O-methyl-*L-glycero-L-talo-*β*-L-manno-*(*E*)-11-tridecenopyranosid]uronate (6b).* To a solution of the crude sample of **4b** (60 mg) in dry benzene (1.2 ml) was added (methoxycarbonylmethylene)triphenylphosphorane (61 mg, 0.182 mmol). The mixture was refluxed for 3 h under argon and then evaporated. The residual syrup was chromatographed on silica gel (7 g) with 6: 1 benzene–ethyl acetate to afford **6b** (56 mg, 84%) as a colorless solid. Recrystallization from ether gave needles of **6b**: 131—133 °C; $[\alpha]_D^{22}$ −34° (*c* 0.88, MeOH); IR (KBr) 1731 and 1662 cm$^{-1}$: $^1$H-NMR δ=0.91−1.12 (12H, m, 4,6,8, and 10-Me), 2.00—2.04 (each 3H, each s, OAc×2), 3.20 (1H, dd, H-3, $J_{2,3}$=3.3 Hz, $J_{3,4}$=10.5 Hz), 3.40 (6H, s, OMe×2), 3.75 (3H, s, COOMe), 4.38 (1H, dd, H-2, $J_{1,2}$=1.1 Hz), 4.96—5.20 (3H, m, H-1,7, and 9), 5.83 (1H, d, H-12, $J_{11,12}$=15.6 Hz), and 6.83 (1H, dd, H-11, $J_{10,11}$=9.0 Hz).

Found: C, 52.50; H, 7.13; Br, 14.38%. Calcd for $C_{24}H_{39}O_9Br$: C, 52.27; H, 7.13; Br, 14.49%.

*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 (6a).* A solution of **6b** (137 mg, 0.248 mmol), tributylstannane (0.080 ml, 0.298 mmol), and AIBN (8 mg, 0.05 mmol) in dry benzene (2.7 ml) was stirred under argon at 60 °C for 3 h, and then the solvent was removed. The residue (300 mg) was chromatographed on silica gel (12 g) with 3: 1 benzene–ethyl acetate to give **6a** (111 mg, 95%) as colorless crystals. Recrystallization from hexane afforded colorless needles: mp 100—101 °C; $[\alpha]_D^{17}$ −61° (*c* 1.22, MeOH); IR (KBr) 1728 and 1653 cm$^{-1}$; $^1$H-NMR δ=0.8−1.1 (12H, m, 4, 6, 8, and 10-Me), 1.41 (1H, ddd, H-2ax, $J_{2ax,2eq}$=11.0 Hz, $J_{2ax,3}$=9.0 Hz, $J_{1,2ax}$=3.6 Hz), 2.00 and 2.04 (each 3H, each s, OAc×2), 3.35 and 3.37 (each 3H, each s, OMe×2), 3.76 (3H, s, COOMe), 4.75—5.25 (3H, m, H-1,7, and 9), 5.84 (1H, d, H-12, $J_{11,12}$=16.0 Hz), and 6.86 (1H, dd, H-11, $J_{10,11}$=8.9 Hz).

Found: C, 60.94; H, 8.37%. Calcd for $C_{24}H_{40}O_9$: C, 61.00; H, 8.53%.

*Methyl [Methyl 2,4,6,8,10,11,12,13,14-Nonadeoxy-7,9-O-isopropylidene-4,6,8, 10, 14-penta-C-methyl-3-O-methyl-*L-manno-*β*-D-galacto-*(11*E*,13*Z*)-11,13-pentadecadienopyranosid]uronate (7a).* To a stirred solution of **1a** (538 mg, 1.26 mmol) and DMP (0.308 ml, 2.52 mmol) in dry acetone (11 ml), was added a 0.1% $H_2SO_4$ solution in acetone (0.54 ml) under ice-cooling. After standing at 0 °C for 3 h, the mixture was neutralized with solid $NaHCO_3$. The insoluble material was filtered and washed with acetone. The filtrate and washings were combined and evaporated. The residual brown syrup (698 mg) was chromatographed on silica gel (22 g) with 10: 1 benzene–ethyl acetate to afford **7a** (583 mg, 99%) as a syrup: $[\alpha]_D^{25}$ −20° (*c* 0.75, MeOH); $UV_{max}$ (EtOH) 266 nm (ε 11400); IR ($CCl_4$) 1705 and 1631 cm$^{-1}$; $^1$H-NMR δ=0.8−1.1 (12H, m, 4,6,8, and 10-Me), 1.27 and 1.30 (each 3H, each s, $CMe_2$), 1.95 (3H, d, 14-Me, $J_{13,Me}$=1.0 Hz), 3.23 (1H, m, H-3, $J_{3,4}$=10.0 Hz), 3.35 (6H, s, OMe×2), 3.76 (3H, s, COOMe), 4.82 (1H, dd, H-1, $J_{1,2ax}$=3.2 Hz, $J_{1,2eq}$=1.4 Hz), 5.98 (1H, dd, H-11, $J_{10,11}$=6.0 Hz, $J_{11,12}$=15.0 Hz), 6.40 (1H, dd, H-13, $J_{12,13}$=11.0 Hz), and 7.16 (1H, dd, H-12).

Found: C, 66.61; H, 9.29%. Calcd for $C_{26}H_{44}O_7$: C, 66.64; H, 9.46%.

*(*R*)-2-Bromo Derivative of 7a (7b).* A sample (205 mg) of **1b** was acetonated by the procedure described in the preparation of **7a** and then worked-up. The crude syrup (281 mg) of **7b** was chromatographed on silica gel (22 g) with 17: 1 benzene–ethyl acetate to afford a pure sample (168 mg, 76%) of **7b** as a syrup: $[\alpha]_D^{27}$ +4° (*c* 0.70, MeOH); $UV_{max}$ (EtOH) 267 nm (ε 23000); IR ($CCl_4$) 1709, 1640, and 1601 cm$^{-1}$; $^1$H-NMR δ=0.88−1.04 (12H, m, 4,6,8, and 10-Me), 1.27 and 1.30 (each 3H, each s, $CMe_2$), 1.96 (3H, s with a little long-range coupling with H-13, 14-Me), 3.20 (1H, dd, H-3, $J_{3,4}$=7.5 Hz, $J_{2,3}$=3.1 Hz), 3.38 (6H, s, OMe×2), 3.76 (3H, s, COOMe), 4.39 (1H, dd, H-2, $J_{1,2}$=1.5 Hz), 4.97 (1H, d, H-1), 5.98 (1H, dd, H-11, $J_{10,11}$=7.0 Hz, $J_{11,12}$=15.4 Hz), 6.40 (1H, dd, H-13, $J_{12,13}$=11.0 Hz), and 7.17 (1H, dd, H-12).

Found: C, 57.32; H, 7.84; Br, 14.37%. Calcd for $C_{26}H_{43}O_7Br$: C, 57.04; H, 7.92; Br, 14.59%.

*Methyl [Methyl 2,4,6,8,10,11,12-Heptadeoxy-7,9-O-isopropylidene-4, 6, 8, 10-tetra-C-methyl-3-O-methyl-*L-manno-*β*-D-galacto-*(*E*)-11-tridecenopyranosid]uronate (9a).* Ozonized oxygen gas containing 1.11 mmol of ozone was passed slowly through a solution of **7a** (260 mg, 0.555 mmol) in dry dichloromethane (13 ml) at −75 °C. To the resulting solution was added dimethyl sulfide (0.1 ml, 5.55 mmol) at the same temperature. The mixture was gradually warmed to room temperature, washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The resulting crude aldehyde **8a** (207 mg) was dissolved in dry benzene (4 ml). To this was added (methoxycarbonylmethylene)triphenylphosphorane (225 mg, 0.675 mmol), and the mixture was refluxed for 4 h under argon. After the removal of the solvent, the residual syrup was chromatographed on silica gel (20 g) with 4 : 1 benzene–ether to afford **9a** (209 mg, 89%) as a colorless syrup: $[\alpha]_D^{27}$ −35° (*c* 0.71, $CHCl_3$); IR ($CCl_4$) 1713 and 1625 cm$^{-1}$: $^1$H-NMR δ=0.8−1.0 (12H, m, 4,6,8, and 10-Me), 1.26 and 1.30 (each 3H, each s, $CMe_2$), 3.37 (6H, s, OMe×2), 3.74 (3H, s, COOMe), 4.8−4.9 (1H, m, H-1), 5.85 (1H, d, H-12, $J_{11,12}$=15.6 Hz), and 7.04 (1H, dd, H-11, $J_{10,11}$=7.2 Hz).

Found: C, 64.56; H, 9.26%. Calcd for $C_{23}H_{40}O_7$: C, 64.46; H, 9.41%.

*(*R*)-2-Bromo Derivative of 9a (9b).* A sample (168 mg) of **7b** was ozonolyzed by the procedure described in preparation of **9a** to afford a crude aldehyde, **8b** (138 mg). A solution of this sample of **8b** (138 mg) and (methoxycarbonylmethylene)triphenylphosphorane (204 mg) in dry benzene (2.9 ml) was refluxed for 5 h under argon. The reaction mixture was then evaporated, and the residue was chromatographed on silica gel (20 g) with 15: 1 benzene–ethyl acetate to give **9b** (109 mg, 70%) as a colorless syrup: $[\alpha]_D^{25}$ −12° (*c* 0.64, MeOH); IR ($CCl_4$) 1728 and 1658 cm$^{-1}$; $^1$H-NMR δ=0.88−1.05 (12H, m, 4,6,8, and 10-Me), 1.27 and 1.30 (each 3H, each s, $CMe_2$), 3.38 (6H, s, OMe×2), 3.37 (3H, s, COOMe), 4.37 (1H, dd, H-2, $J_{2,3}$=3.2 Hz, $J_{1,2}$=1.5 Hz), 4.97 (1H, d, H-1), 5.83 (1H, dd, H-12, $J_{11,12}$=15.9 Hz, $J_{10,12}$=1.0 Hz), and 7.01 (1H, dd, H-11, $J_{10,11}$=7.3 Hz).

Found: C, 54.22; H, 7.64; Br, 15.47%. Calcd for $C_{23}H_{39}$-

O$_7$Br: C, 54.44; H, 7.75; Br, 15.75%.

*Methyl 2,4,6,8,10,11,12-Heptadeoxy-7,9-O-isopropylidene-4,6,8,10-tetra-C-methyl-3-O-methyl-*L-manno-β-D-galacto-*(E)-11-tridecenopyranoside-(1,5)(**10a**).* *(A)*: A 27.5 (W/W)% DIBAL in hexane (0.460 ml, 0.803 mmol) was added dropwise to a stirred cooled solution (−75 °C) of **9a** (172 mg, 0.401 mmol) in dry toluene (17.2 ml). Once the addition of the DIBAL was complete, the reaction mixture was stirred at −75 °C for 30 min. It was then warmed to 0 °C, and to this mixture 50% aqueous acetic acid (0.08 ml) and ethyl acetate (4 ml) were added successively. The resulting insoluble matter was filtered through Celite and washed with ethyl acetate. The combined filtrate and washings were evaporated. The residual syrup (180 mg) was chromatographed on silica gel (8 g) with 2 : 1 benzene–ethyl acetate to afford **10a** (112 mg, 70%) as a colorless syrup: $[\alpha]_D^{25}$ −30° (*c* 1.16, CHCl$_3$); $^1$H-NMR $\delta$=0.8−1.0 (12H, m, 4,6,8, and 10-Me), 1.29 and 1.33 (each 3H, each s, CMe$_2$), 2.23 (1H, ddd, H-2eq, $J_{2eq,2ax}$=13.1 Hz, $J_{2eq,3}$=4.7 Hz, $J_{1,2eq}$=1.6 Hz), 3.40 (6H, s, OMe×2), 4.0—4.2 (2H, m, H-13×2), 4.86 (1H, dd, H-1, $J_{1,2ax}$=4.0 Hz), and 5.7—5.8 (2H, m, H-11 and 12).

Found: C, 66.22; H, 9.87%. Calcd for $C_{22}H_{40}O_6$: C, 65.97; H, 10.07%.

*(B)*: To a stirred solution of **6a** (75 mg, 0.158 mmol) in dry toluene (3.7 ml) was added dropwise 27.5% DIBAL in hexane (0.040 ml, 0.07 mmol) at −75 °C. After being stirred at the same temperature for 10 min, the reaction mixture was warmed to 0 °C and treated with a 50% aqueous acetic acid (0.079 ml) and ethyl acetate (1 ml). After the removal of the resulting insoluble matter by filtration, the filtrate was evaporated to give a colorless syrup (52 mg, 92%) of the triol. A mixture of the crude triol (52 mg), DMP (0.036 ml, 0.29 mmol), and dry DMF (0.52 ml) was stirred at room temperature for 5 h. The mixture was then neutralized with triethylamine and evaporated. The residue was chromatographed on silica gel (5 g) with 2 : 1 benzene–ethyl acetate to afford **10a** (43 mg, 73%).

*(R)-2-Bromo Derivative of **10a** (**10b**).* A solution of **9b** (96 mg, 0.189 mmol) in dry toluene (9.6 ml) was treated with a 27.5% DIBAL in hexane (0.215 ml, 0.378 mmol) at −75 °C for 10 min and then worked-up by the procedure described in the preparation of **10a** from **9a**. The crude syrup of **10b** (108 mg) thus obtained was chromatographed on silica gel (10 g) with 3: 1 benzene–ethyl acetate to afford a colorless syrup of **10b** (87 mg, 96%): $[\alpha]_D^{22}$ −7° (*c* 1.40, MeOH); $^1$H-NMR $\delta$=0.89−1.03 (12H, m, 4,6,8, and 10-Me), 1.27 and 1.31 (each 3H, each s, CMe$_2$), 3.20 (1H, dd, H-3, $J_{3,4}$=7.1 Hz, $J_{2,3}$=3.1 Hz), 3.39 (6H, s, OMe×2), 4.0—4.2 (2H, m, H-13×2), 4.39 (1H, dd, H-2, $J_{1,2}$=1.5 Hz), 4.98 (1H, d, H-1), and 5.65—5.79 (2H, m, H-11 and 12).

Found: C, 54.89; H, 7.98; Br, 16.38%. Calcd for $C_{22}H_{39}O_6Br$: C, 55.11; H, 8.20; Br, 16.67%.

*Methyl 2-Bromo-2,4,6,8,10,11,12-heptadeoxy-7,9-O-isopropylidene-4,6,8,10-tetra-C-methyl-3-O-methyl-*L-glycero-L-talo-β-L-manno-*(E)-11-tridecenodialdopyranoside-(1,5) (**11b**).* A mixture of chromium trioxide (71 mg, 0.716 mmol) and dry HMPA (0.21 ml) was stirred at room temperature for 2.5 h, and a solution of **10b** (172 mg, 0.358 mmol) in HMPA (0.34 ml) was then added. Stirring was continued for 1 week at room temperature, after which the mixture was poured into ice water and extracted with ether. The ether layer was washed successively with a 5% aqueous NaOH solution, water, and a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (8.3 g) with 10 : 1 benzene–ethyl acetate to give **11b** (106 mg, 62%) as a colorless crystal. Recrystallization from ether–petroleum ether afforded colorless needles of **11b**: mp 129—130 °C; $[\alpha]_D^{25}$ −10° (*c* 0.96, MeOH); IR (KBr) 1689 and 1634 cm$^{-1}$; $^1$H-NMR $\delta$=0.94, 0.98, 1.01, and 1.05 (each 3H, each d, 4,6,8, and 10-Me, $J$=6—7 Hz), 1.27 and 1.32 (each 3H, each s, CMe$_2$), 3.23 (1H, dd, H-3, $J_{2,3}$=3.1 Hz, $J_{3,4}$=9.9 Hz), 3.39 (6H, s, OMe×2), 4.40 (1H, dd, H-2, $J_{1,2}$=1.6 Hz), 4.98 (1H, d, H-1), 6.14 (1H, ddd, H-12, $J_{11,12}$=15.9 Hz, $J_{12,13}$=7.7 Hz, $J_{10,12}$=1.0 Hz), 6.96 (1H, dd, H-11, $J_{10,11}$=6.5 Hz), and 9.53 (1H, d, H-13).

Found: C, 55.38; H, 7.64; Br, 16.50%. Calcd for $C_{22}H_{37}O_6Br$: C, 55.35; H, 7.81; Br, 16.74%. On column chromatography, unchanged **10b** (37 mg, 22%) was recovered.

*13E-Isomer of **7b** (**7′b**); Condensation of **11b** with **14**.* To an ice-cooled suspension of NaH (3.6 mg, 0.082 mmol; 55% dispersion in mineral oil) in dry THF (0.27 ml), **14**[13] (15 mg, 0.074 mmol) was added, and the mixture was stirred at room temperature for 1 h. It was then cooled to −75 °C, and a solution of **11b** (29.6 mg, 0.062 mmol) in dry THF (0.3 ml) was added. Stirring was continued at −60—−65 °C for 1 h. The reaction mixture was then poured into ice water and extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was preparatively thin-layer chromatographed on Merck Kieselgel 60-F$_{254}$ (0.5 mm) with 25 : 1 and 30 : 1 benzene–ethyl acetate (two passes), to afford **7b** (0.5 mg, 1.5%) and **7′b** (28 mg, 83%): $[\alpha]_D^{20}$ 0° (*c* 0.78, MeOH); UV$_{max}$ (EtOH) 266 nm ($\varepsilon$ 28800); IR (CCl$_4$) 1711 and 1641 cm$^{-1}$; $^1$H-NMR $\delta$=0.88−1.05 (12H, m, 4,6,8, and 10-Me), 1.27 and 1.30 (each 3H, each s, CMe$_2$), 1.94 (3H, d, 14-Me, $J_{13,Me}$=1.0 Hz), 3.20 (1H, dd, H-3, $J_{3,4}$=7.1 Hz, $J_{2,3}$=3.0 Hz), 3.38 (6H, s, OMe×2), 3.77 (3H, s, COOMe), 4.38 (1H, dd, H-2, $J_{1,2}$=1.6 Hz), 4.97 (1H, d, H-1), 6.03 (1H, dd, H-11, $J_{11,12}$=15.0 Hz, $J_{10,11}$=6.0 Hz), 6.42 (1H, dd, H-12, $J_{12,13}$=10.0 Hz), and 7.19 (1H, dd, H-13).

Found: C, 57.37; H, 7.97; Br, 14.26%. Calcd for $C_{26}H_{43}O_7Br$: C, 57.04; H, 7.92; Br, 14.59%.

*Allylic Bromide (**12a**) and Triphenylphosphonium Salt (**13a**).* Triethylamine (0.05 ml, 0.315 mmol) and lithium bromide (20 mg, 0.23 mmol) were added to a solution of **10a** (83 mg, 0.21 mmol) in dichloromethane (1.6 ml), and then the new mixture was cooled at 0 °C. To this cooled suspenion, mesyl chloride (0.02 ml, 0.24 mmol) was added under stirring. Stirring was continued at 0 °C for 1 h at room temperature for 12 h. The reaction mixture was then diluted with acetone, and the precipitates were filtered off using Celite and washed with ethyl acetate. The filtrate and washings were combined and evaporated to afford a yellow syrup. The syrup was chromatographed on silica gel (Kieselgel 60, 8 g) with 9: 1 hexane–ethyl acetate to give **12a** (77 mg, 80%) as a colorless crystalline solid: $^1$H-NMR $\delta$=0.8−1.0 (12H, m, 4, 6, 8, and 10-Me), 1.28 and 1.32 (each 3H, each s, CMe$_2$), 3.36 (6H, s, OMe×2), 3.9—4.0 (2H, doublet like, H-13 and 13′), 4.85 (1H, m, H-1), and 5.7—5.9 (2H, m, H-11 and 12). A solution of **12a** (30 mg, 0.06 mmol) and triphenylphosphine (17 mg, 0.065 mmol) in dry ether (0.3 ml) was stirred under argon at 30 °C for 2 d. The resulting solid was separated from ether by decantation and triturated with ether to afford a colorless powder of **13a** (46.5 mg, 100%); IR (KBr) 1430, 1110, 1000, 730, and 710 cm$^{-1}$.

*Allylic Bromide (**12b**) and Triphenylphosphonium Salt (**13b**).* By the procedure described in the preparation of **12a**, a sample (91 mg) of **10b** was converted into a crude bromide ,**12b**, which was then purified by column chromatography, using Kieselgel 60 (10 g) with 50: 1 benzene–ethyl acetate, to afford a practically pure sample of **12b** (93 mg, 90%) as colorless needles: mp 126—127 °C; $^1$H-NMR $\delta$=0.97 (doublet like, 12H, 4, 6, 8, and 10-Me), 1.27 and 1.31 (each 3H, each s, CMe$_2$), 3.20 (1H, dd, H-3, $J_{2,3}$=3.5 Hz, $J_{3,4}$=6.6 Hz), 3.40 (6H, s, OMe × 2), 4.40 (1H, dd, H-2, $J_{1,2}$ = 1.6 Hz), 4.99 (1H, d, H-1), and 5.69—5.87 (2H, m, H-11 and 12). A solution of **12b** (92 mg, 0.17 mmol) and triphenylphosphine (89 mg, 0.339 mmol) in dry benzene (0.28 ml) was stirred under arogn at 55 °C for 5 d. After the subsequent removal of the solvent by evaporation, the resulting solid was washed with hexane by trituration to afford a colorless powder of **13b** (136 mg, 100%): IR (KBr) 1440, 1118, 998, and 724 cm$^{-1}$.

*Wittig Condensation of Methyl Pyruvate with Triphenylphosphorane Generated from **13a** or **13b**.* *(A)* : A 1.6 M butyllithium in hexane (0.027 ml, 0.043 mmol) was added, under argon, to a stirred, cooled solution (−75 °C) of **13a** (46.5 mg, 0.064 mmol) in dry THF (0.5 ml). After the solution had been stirred at −75 °C for 1 h, to the deep red solution was added a solution of methyl pyruvate (4.4 mg, 0.043 mmol) in dry THF (0.1 ml). Stirring was continued at −75 °C for 0.5 h, and then it was evaporated. Ether was added to the residual syrup, and the precipitates were filtered off and washed with ether. The combined filtrate and washings were then evaporated to afford a yellow syrup (40.3 mg). The crude product was purified by PLC with 10 : 1 benzene–ethyl acetate to give a mixture of **7a** and its 13*E*-isomer, **7′a**(11.9 mg). The mixture was chromatographed on alumina (Woelm grade I, 1 g) with 3: 1 benzene–chloroform to afford **7a** [$R_f$ 0.51 (2: 1 hexane–ether, two passes)] as a colorless syrup [4 mg (28%)] and **7′a** [$R_f$ 0.49 (2: 1 hexane–ether, two passes)], also as a colorless syrup [5 mg (34%)]: $[\alpha]_D^{30}$ −9° (*c* 1.29, MeOH); UV$_{max}$ (EtOH) 266 nm (ε 35700); IR ($CCl_4$) 1709 and 1641 cm$^{-1}$; $^1$H-NMR δ=0.85—1.05 (12H, m, 4, 6, 8, and 10-Me), 1.27 and 1.31 (each 3H, each s, $CMe_2$), 1.95 (3H, d, 14-Me, $J_{13,Me}$=1.5 Hz), 3.34 (6H, s, OMe × 2), 3.75 (3H, s, COOMe), 4.81 (1H, dd, H-1, $J_{1,2ax}$=3.5 Hz, $J_{1,2eq}$=1.5 Hz), 6.4 (1H, dd, H-11, $J_{11,12}$=14.6 Hz, $J_{10,11}$=6.2 Hz), 6.40 (1H, dd, H-12, $J_{12,13}$=10.0 Hz), and 7.17 (1H, dd, H-13).

Found: C, 66.37; H, 9.45%. Calcd for $C_{26}H_{44}O_7$: C, 66.64; H, 9.46%.

*(B)*: A 1.6 M butyllithium in hexane (0.089 ml) was added, under argon, to a stirred, cooled solution (−75 °C) of **13b** (77 mg) in dry THF (0.77 ml). After the mixture had been stirred at −75 °C for 15 min, methyl pyruvate (19 mg) was added to the deep-red solution. The solution immediately turned pale yellow. It was then poured into ice-cooled water, and the mixture was extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue (116 mg) was preparatively thin-layer chromatographed on two PLC plates (in two passes) with 25: 1 and 30: 1 benzene–ethyl acetate to afford **7b** [$R_f$ 0.47 (15: 1 benzener–ethyl acetate)] as a pale yellow viscous syrup [21 mg (40%)] and **7′b** [$R_f$ 0.42 (15: 1 benzene–ethyl acetate)] also as a pale yellow viscous syrup [22 mg (42%)]; these two substances were found by $^1$H-NMR analysis and TLC to be identical with the corresponding authentic samples.

*Methyl [Methyl 2,4,6,8,10,11,12,13,14-Nonadeoxy-4,6,8,10,14-penta-*C*-methyl-*3-O*-methyl-*L-manno-*β*-D-galacto*(11*E*, 13*Z*)-11,13-pentadecadienopyranosid]uronate (**1a**).* A sample of **7a** (15 mg) was dissolved in 50 (v/v)% aqueous DFA (0.15 ml), after which the mixture was stand at 0 °C for 25 min. The solution was then neutralized with solid $NaHCO_3$ and extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. Chromatographic purification using silica gel (1 g) with 3: 2 benzene–ethyl acetate afforded **1a** (11 mg, 80%) as a colorless syrup; this syrup was identical with the authentic sample.

*(R)-2-Bromo Derivative of **1a** (**1b**).* A solution of **7b** (27 mg) in 90 (v/v) % TFA (0.27 ml) was kept at 0 °C for 15 min. The subsequent removal of the solvent, followed by column chromatography on silica gel (2.5 g) with 3: 1 benzene–ethyl acetate, gave a pale yellow syrup of **1b** (25 mg, 100%), whose $^1$H-NMR, IR, and UV spectra were identical with those of the authentic sample.

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## References

1) Part II: M. Nakata, Y. Ikeyama, H. Takao, and M. Kinoshita, *Bull. Chem. Soc. Jpn.*, **53**, 3252 (1980).

2) M. Kinoshita, K. Tatsuta, and M. Nakata, *J. Antibiot.*, **31**, 630 (1978).

3) The acetylation of **1b** with acetic anhydride in pyridine also gave **3b** in a 94% yield after it had been kept at 45 °C for 7 d.

4) J. J. Pappas, W. P. Keaveney, E. Gancher, and M. Berger, *Tetrahedron Lett.*, **1966**, 4273.

5) The **6a** could be derived directly from the synthetic sample of **4a** in a good yield; see the following paper.

6) G. Cardillo, M. Orena, and S. Sandri, *Synthesis*, **1976**, 394.

7) A. I. Meyers, K. Tomioka, D. M. Roland, and D. Comins, *Tetrahedron Lett.*, **1978**, 1375; E, J, Corey, L. O. Weigel, D. Floyd, and M. G. Bock, *J. Am. Chem. Soc.*, **100**, 2916 (1978).

8) H. O. House and G. H. Rasmusson, *J. Org. Chem.*, **26**, 4278 (1961).

9) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970); D. A. Evans, C. E. Sacks, R. A. Whitney, and N. G. Mandel, *Tetrahedron Lett.*, **1978**, 727; E. W. Collington and A. I. Meyers, *J. Org. Chem.*, **36**, 3044 (1971).

10) E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, **1979**, 2317.

11) K. B. Becker, *Helv. Chim. Acta*, **60**, 68 (1977), and the references cited therein.

12) M. Schlosser, *Topics in Stereochemistry*, **5**, 1 (1970).

13) The reagent **14** [bp 110—115 °C (10 mmHg)] was prepared according to the procedure used for the preparation of diethyl [1-(ethoxycarbonyl)ethyl]phosphonate described by Wadsworth: W. S. Wadsworth, Jr., *Org. React.*, **25**, 142 (1977).