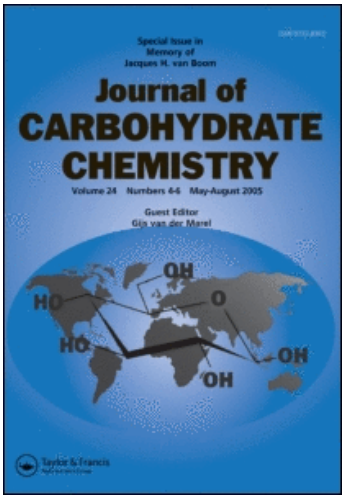

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Facile Syntheses of Some L-Sugar Derivatives from L-Quebrachitol

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FACILE SYNTHESES OF SOME L-SUGAR DERIVATIVES FROM L-QUEBRACHITOL

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ABSTRACT

Naturally occurring optically active cyclitol, L-quebrachitol (1) was transformed into 5-*O*-methyl L-manno- (5) and L-talofuranose derivatives (11) and methyl L-guluronate derivative (15) in short step reactions.

INTRODUCTION

L-Quebrachitol (1), one of the optically active cyclitols readily obtained from serum of the rubber tree,[1] has attracted attention as a useful starting material for synthesis of natural products in an enantiomerically pure form. Syntheses of optically active cyclitols,[2] branched-chain cyclitols,[3] inositol phosphates,[4] fluorinated inositols,[5] aldohexoses,[1b] and other natural products[6] starting from 1 have been reported. In this publication, as part of our synthetic studies utilizing L-quebrachitol as a useful starting material and as a valuable resource,[1b,6] we wish to report a facile conversion of 1 into aldohexoses having L-manno (5) and L-talo (11) configurations, and into a L-guluronic acid derivative (15). These L-sugars were prepared by oxidative ring opening of the cyclohexane ring of 1.

RESULTS AND DISCUSSION

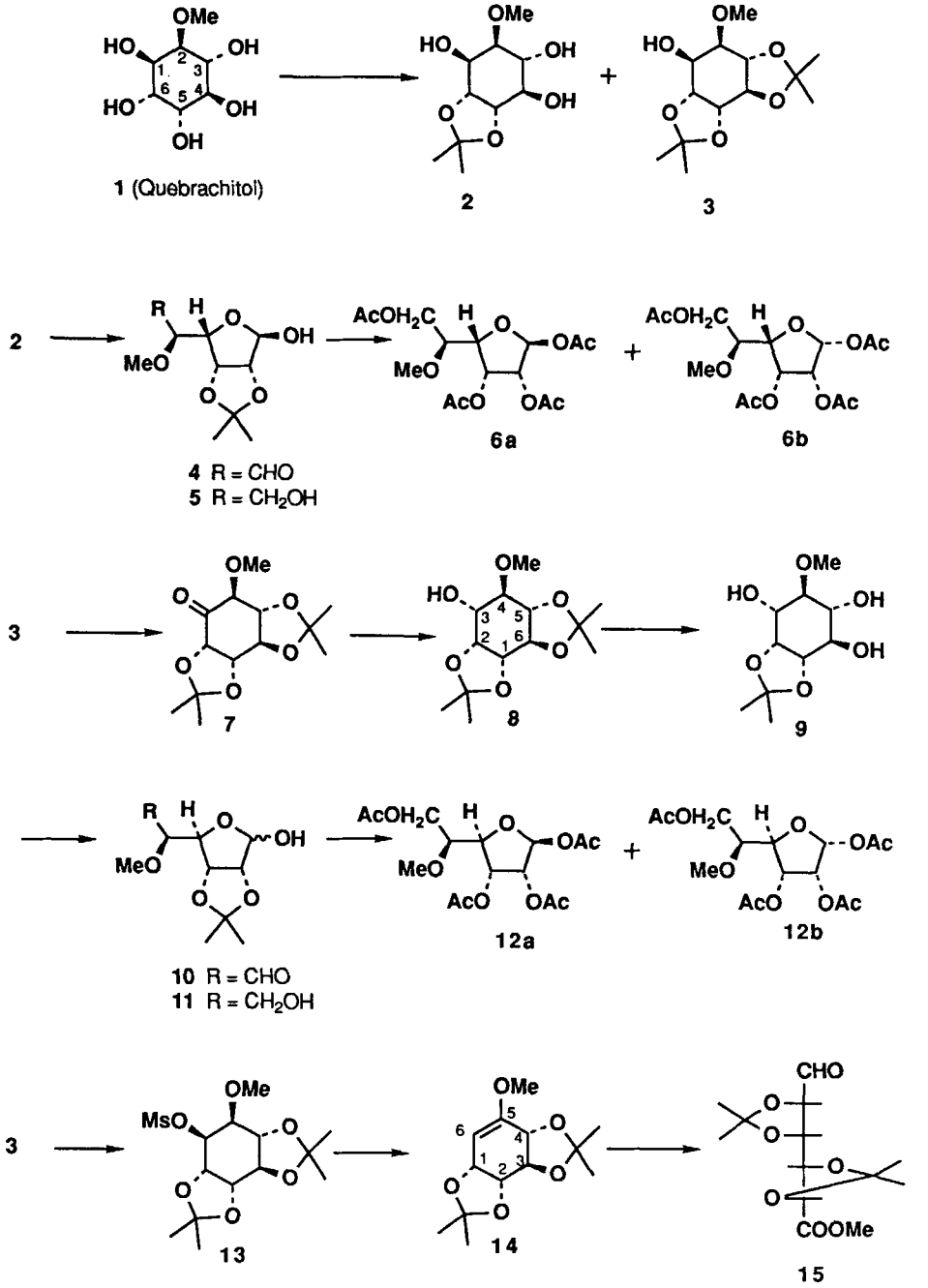
Treatment of L-quebrachitol (1) with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide (DMF) in the presence of *p*-toluenesulfonic acid gave the known crystalline

acetonide products (**2**) and (**3**)[3a] in 22 and 40 % yields, respectively. Periodate oxidation of **2** in acetone-water afforded a dialdose, one of the aldehyde groups of which formed the hemiacetal to give **4** (SCHEME 1). Without isolation, the free aldehyde function of **4** was selectively reduced with sodium borohydride in methanol to provide crystalline 2,3-*O*-isopropylidene-5-*O*-methyl-L-mannofuranose (**5**) in 60% yield from **2**. ^{1}H NMR analysis of **5** revealed that **5** was the sole product and the anomeric configuration was assigned to be α ($J_{1,2}$ = 0 Hz).[7] Acid hydrolysis and subsequent acetylation afforded a mixture of 1,2,3,6-tetra-*O*-acetyl-5-*O*-methyl-α- (**6a**) and β-L-mannofuranose (**6b**) in 79 % yield. In the ^{1}H NMR spectrum, the anomeric protons were observed at δ 6.19 (doublet, J = 3.9 Hz) and at δ 6.32 (doublet, J = 4.8 Hz) in a ratio of 6:1. Judging from the coupling constants and chemical shifts of the anomeric protons, it was assumed that the major isomer is the α-anomer (**6a**).[7] From this mixture, pure **6a** was isolated in 32 % yield after silica gel chromatography.

On the other hand, compound **3** was oxidized with RuO_4 to afford the known ketone (**7**)[3a] in 94% yield, which was then reduced with sodium borohydride to give the inverted alcohol (**8**) in 99 % yield as a single product. Removal of the *trans O*-isopropylidene group afforded **9** (65 % yield), which was then treated with sodium periodate, followed by reduction of the resulting free aldehyde group to give 2,3-*O*-isopropylidene-5-*O*-methyl-L-talofuranose (**11**) as an anomeric mixture in 81% yield from **9**. ^{1}H NMR analysis showed that **11** was a 9:1 mixture of α- and β-anomers (α-anomer, δ 5.28, $J_{1,2}$ = 0; β-anomer, δ 5.42, $J_{1,2}$ = 3.9 Hz).[7] Acid hydrolysis of **11**, followed by acetylation provided a mixture of 1,2,3,6-tetra-*O*-acetyl-5-*O*-methyl-α- (**12a**) and β-L-talofuranose (**12b**) in 80 % yield. The ^{1}H NMR of this mixture showed that the ratio of **12a** and **12b** was 3:1 (anomeric proton of **12a**, δ 6.12, J = 1.5 Hz; **12b**, δ 6.43, J = 4.0 Hz).[7] From this mixture, pure **12a** was isolated in 24% yield from **11**.

Compound **3** was mesylated with methanesulfonyl chloride to give the mesylate (**13**) in 97 % yield. Treatment of **13** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded the vinyl ether (**14**) in 58 % yield. Ozonolysis of **14**, followed by reductive work-up provided methyl 2,3:4,5-di-*O*-isopropylidene-L-guluronate (**15**), the compound of structural interest because it is a rare example of an open-chain *aldehydo* uronic acid derivative, in 86 % yield.

^{1}H and ^{13}C NMR data for compounds **5**, **6a**, **11**, **12a** and **15** are shown in Table 1. For a further confirmation of the structure of **5**, deprotection of the methyl ether in **6a** was attempted (SCHEME 2). Treatment of **6a** with CrO_3 in acetic acid[9] at 50 °C oxidized the methyl ether as well as the anomeric carbon to afford a formyl lactone (**16**) in 87 % yield. Reduction of **16** with diisobutylaluminum hydride and subsequent acid treatment, followed by conventional acetylation, provided methyl 2,3,4,6-tetra-*O*-acetyl-α-L-manno-

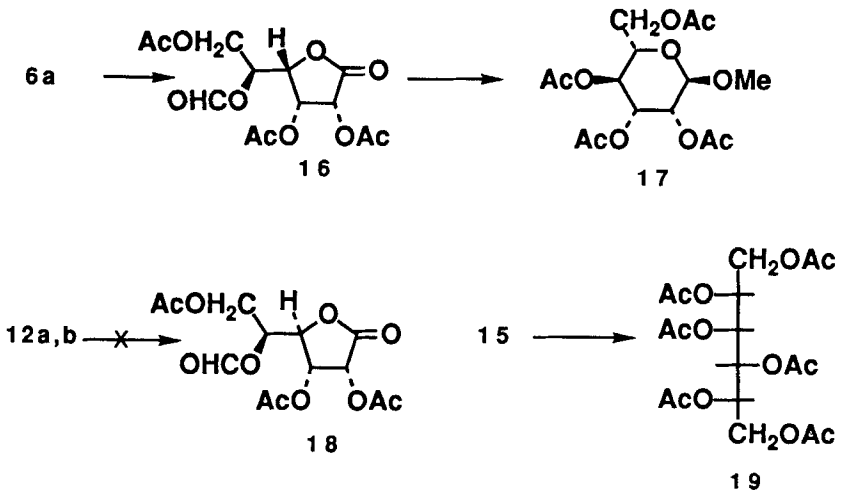


SCHEME 1

TABLE 1. ^{1}H and ^{13}C NMR Data for Compounds 5, 6a, 11, 12a and 15.

	5	6a	11[a]	12a	15
^{1}H NMR[b]					
H-1	5.34 (s)	6.19 (d)	5.28 (s)	6.12 (d)	9.73 (d)
$J_{1,2}$	0	3.9	0	1.5	2.0
H-2	4.59 (d)	5.43 (dd)	4.51 (d)	5.31 (dd)	4.51 (dd)
$J_{2,3}$	5.9	4.9	5.9	4.9	8.3
H-3	4.81 (dd)	5.62 (dd)	4.74 (d)	5.50 (dd)	4.62 (dd)
$J_{3,4}$	3.4	3.4	0	6.8	1.5
H-4	4.19 (dd)	4.34 (dd)	4.48 (d)	4.26 (dd)	4.17 (dd)
$J_{4,5}$	8.8	8.3	2.4	3.9	8.3
H-5	3.57 (ddd)	3.62 (ddd)	3.40 (m)	3.46 (ddd)	4.61 (d)
$J_{5,6}$	2.9	2.4	4.9	5.4	
$J_{5,6'}$	2.4	4.4	3.4	5.4	
H-6	3.92 (dd)	4.64 (dd)	3.94 (dd)	4.25 (dd)	---
$J_{6,6'}$	11.7	12.2	12.0	11.5	
H-6'	3.71 (dd)	4.02 (dd)	3.85 (dd)	4.15 (dd)	---
OCH_3	3.46 (s)	3.36 (s)	3.56 (s)	3.51 (s)	3.82 (s)
OAc	---	2.07, 2.09, 2.10, 2.15	---	2.07, 2.08, 2.09, 2.13	---
CMe_2	1.33 (s, 3H) 1.44 (s, 3H)	---	1.32 (s, 3H) 1.48 (s, 3H)	---	1.39 (s, 3H) 1.43 (s, 3H) 1.46 (s, 3H) 1.62 (s, 3H)
^{13}C NMR[c]	24.8, 26.3, 57.8, 60.6, 78.0, 78.3, 79.8, 85.4, 100.9, 112.3.	20.3, 20.5, 20.8, 21.0, 58.0, 62.0, 71.2, 75.6, 76.0, 77.9, 98.3, 169.2, 169.4, 169.6, 170.7.	24.8, 26.4, 58.1, 60.8, 79.8, 82.4, 87.1, 88.2, 104.2, 112.1.	20.3, 20.5, 20.8, 21.0, 59.3, 62.6, 70.1, 74.1, 77.8, 81.1, 97.9, 169.3, 169.5, 169.8, 170.6.	25.1, 25.9, 26.4, 26.8, 52.5, 74.9, 76.1, 76.4, 80.7, 111.4, 111.7, 170.4, 201.4.

a. Signals for the major isomer are shown.
b. Measured in $CDCl_3$ solution at 270 MHz. Chemical shifts are relative to Me_4Si (0 ppm) and coupling constants (J) are expressed in Hz.
c. Measured in $CDCl_3$ solution at 67 MHz. Chemical shifts are relative to $CDCl_3$ (77.0 ppm).



SCHEME 2

pyranoside (**17**) in 38 % isolated yield. The ^{1}H NMR spectrum of **17** was identical with that of methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside,[10] and the specific rotation of **17** ([α]$_D$ -35 °) was almost equal in value but opposite in sign in comparison to that of the D-isomer ([α]$_D$ +36 °). Unfortunately, similar oxidation of the β-anomer (**6b**) and the L-talo derivatives (**12a,b**) afforded many unidentified products and the desired compounds (**16** and **18**) could not be isolated. On the other hand, compound **15** was reduced with $LiAlH_4$ and then treated with *p*-toluenesulfonic acid in methanol. Acetylation of the product afforded hexa-*O*-acetyl-D-glucitol (**19**) in 61 % yield from **15**. The spectral (^{1}H NMR and IR) and physical (mp and [α]$_D$) properties of **19** were identical with those of the authentic sample[12] prepared from D-glucitol.

Thus, properly protected L-sugar derivatives (**5**, **11**, and **15**) were prepared from **1** in short reaction steps (less than 6 steps) and in good overall yields. These compounds, having masked or naked aldehyde functions, should be useful starting materials for chiral syntheses of natural products possessing polyhydroxyl functions[14] such as higher carbon sugars.

EXPERIMENTAL

General Procedures. Melting points were determined with Mitamura Riken micro hot stage and are uncorrected. Specific rotations were measured in a 0.1 dm tube with a

Jeol DIP-370 polarimeter. ^1H NMR spectra were recorded with Jeol JNM-GX 400 (400 MHz), GX-270 (270 MHz), or EX-90 (90 MHz) spectrometer in chloroform-*d* with tetramethylsilane as an internal standard, unless otherwise noted. ^{13}C NMR spectra were taken with GX-270 spectrometer. IR spectra were recorded with a Jasco IR-810 spectrometer.

Organic solutions were dried over anhydrous sodium sulfate and concentrated below 40 °C under reduced pressure.

2,3-*O*-Isopropylidene-5-*O*-methyl-α-L-mannofuranose (5). To a stirred solution of 1L-5,6-di-*O*-isopropylidene-2-*O*-methyl-*chiro*-inositol[3a] (**2**, 2.01 g, 8.58 mmol) in acetone-water (5:1, 60 mL) at 0 °C was added aqueous solution (40 mL) of sodium periodate (8.72 g, 40.8 mmol) dropwise. The pH of the reaction mixture was maintained at 6~7 by adding solid sodium hydrogencarbonate. After being stirred at 0 °C for 2.5 h, the mixture was partially concentrated to remove acetone, and extracted with ethyl acetate. The extract was washed with brine and dried. Evaporation of the solvent gave crude **4** as a colorless syrup. This crude **4** was dissolved in methanol (60 mL). To this solution at 0 °C was added sodium borohydride (227 mg, 6.01 mmol) in several portions. After all the starting material was consumed (tlc monitoring, 1:1 ethyl acetate-toluene), the reaction was quenched by adding IR-120B resin (H^+ form). The insoluble materials were removed by filtration and the filtrate was concentrated to give a crystalline residue, which was recrystallized from acetone to give 1.21 g (60 % from **2**) of compound **5** as needles: mp 99.0-100.5 °C, $[\alpha]_D^{28}$ -20 ° (*c* 1.2, $CHCl_3$); IR (KBr) 3430 cm^{-1}; ^1H and ^{13}C NMR data are given in Table 1.

Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.20; H, 7.55.

1,2,3,6-Tetra-*O*-acetyl-5-*O*-methyl-α-L-mannofuranose (6a) and its β-Anomer (6b). A solution of compound **5** (207 mg, 0.884 mmol) in tetrahydrofuran (4 mL) and 1 mol dm^{-3} aqueous sulfuric acid (2 mL) was heated at 50 °C for 2 h. The reaction mixture was neutralized with solid sodium hydrogencarbonate and concentrated to give a residue, which was dissolved in acetic anhydride (2 mL) and pyridine (2 mL). After being stirred at room temperature for 5 h, the mixture was concentrated, then diluted with ethyl acetate. The resulting solution was washed successively with 1 mol dm^{-3} aqueous HCl solution, saturated sodium hydrogencarbonate solution and brine, then dried. Evaporation of the solvent left a syrup, which was chromatographed on a column of silica gel (5 g) with ethyl acetate-toluene (1:10) as eluant to give 120 mg (32%) of compound **6a** as a colorless syrup: $[\alpha]_D^{21}$ -70 ° (*c* 1.3, $CHCl_3$); IR (neat) 1750 cm^{-1}; ^1H and ^{13}C NMR data are given in Table 1.

Anal. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.89; H, 6.10.

Further elution gave 150 mg (47%) of a mixture of **6a** and **6b** (3.2:1) as a colorless syrup: ^{1}H NMR for **6b**, δ 2.02, 2.06, 2.08, 2.14 (4s, 12H, 4OAc), 3.32 (s, 3H, OMe), 3.58 (m, 1H, H-5), 3.95 (dd, 1H, $J_{5,6}$ = 3.9, $J_{6,6'}$ = 12.3 Hz, H-6), 4.20 (dd, 1H, $J_{3,4}$ = 4.7, $J_{4,5}$ = 9.2 Hz, H-4), 4.67 (dd, 1H, $J_{5,6'}$ = 2.8 Hz, H-6'), 5.23 (dd, 1H, $J_{1,2} = J_{2,3}$ = 4.8 Hz), 5.59 (dd, 1H, H-3), 6.32 (d, 1H, H-1).

1D-1,2:5,6-Di-*O*-isopropylidene-4-*O*-methyl-*myo*-inositol (8). To a solution of 2L-(2,3,5/4,6)-2,3:4,5-di-*O*-isopropylidene-6-*O*-methyl-pentahydroxycyclohexanone (**7**),[3a] prepared from compound **3** by the method reported by Paulsen,[3a] (167 mg, 0.614 mmol) in methanol (4 mL) at 0 °C was added sodium borohydride (24 mg, 0.64 mmol). After being stirred at 0 °C for 40 min, the mixture was concentrated, then diluted with ethyl acetate. The organic layer was washed with brine and dried. Evaporation of the solvent left a syrup, which was purified on a column of silica gel (3 g) with ethyl acetate-toluene (1:3) as eluant to give 167 mg (99%) of compound **8** as a colorless syrup: $[\alpha]_D^{28}$ +10 ° (*c* 1.0, $CHCl_3$); IR (neat) 3500 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.39, 1.43, 1.45, 1.55 (4s, 12H, $2CMe_2$), 2.59 (b, 1H, OH), 3.47 (dd, 1H, $J_{4,5}$ = 7.8, $J_{5,6}$ = 10.7 Hz, H-5), 3.51 (s, 3H, OMe), 3.67 (dd, 1H, $J_{3,4}$ = 2.4 Hz, H-4), 3.97 (m, 1H, H-3), 4.16 (dd, 1H, $J_{1,6}$ = 7.3 Hz, H-6), 4.34 (dd, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 4.42 (dd, 1H, $J_{2,3}$ = 3.4 Hz, H-2).

Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.93; H, 7.77.

1D-1,2-*O*-Isopropylidene-4-*O*-methyl-*myo*-inositol (9). A mixture of compound **8** (767 mg, 2.80 mmol) and *p*-toluenesulfonic acid monohydrate (5.3 mg, 0.028 mmol) in methanol (12 mL) was stirred at 0 °C for 4 h. The reaction mixture was neutralized with triethylamine and then concentrated to give a residue, which was chromatographed on a column of silica gel (15 g) with chloroform-methanol (10:1) as eluant to afford 427 mg (65%) of compound **9** as a crystalline residue: mp 132-133 °C (from ethanol); $[\alpha]_D^{24}$ -25 ° (*c* 2.7, MeOH); IR (KBr) 3450 cm^{-1}; ^{1}H NMR (270 MHz, CD_3OD) δ 1.35, 1.51 (2s, 6H, CMe_2), 3.20 (dd, 1H, $J_{1,6}$ = 8.8, $J_{5,6}$ = 9.0 Hz, H-6), 3.24 (dd, 1H, $J_{4,5}$ = 9.3 Hz, H-5), 3.59 (dd, 1H, $J_{3,4}$ = 7.3 Hz, H-4), 3.60 (s, 3H, OMe), 3.74 (dd, 1H, $J_{1,2}$ = 4.4 Hz, H-1), 3.91 (dd, 1H, $J_{2,3}$ = 5.4 Hz, H-3), 4.32 (dd, 1H, H-2).

Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.03; H, 7.43.

2,3-*O*-Isopropylidene-5-*O*-methyl-L-talofuranose (11). To a solution of compound **9** (500 mg, 2.13 mmol) in acetone-water (2:1, 9 mL) at 0°C was added an aqueous solution (6 mL) of sodium periodate (911 mg, 4.26 mmol) dropwise. The pH of the reaction mixture was maintained at 6~7 by adding solid sodium hydrogencarbonate. After being stirred at 0 °C for 20 min, the mixture was partially concentrated to remove acetone, and extracted with ethyl acetate. The extract was washed with brine and dried. Evaporation of the

solvent gave crude **10** as a colorless syrup. This crude **10** was dissolved in methanol (8 mL). To this solution at 0 °C was added sodium borohydride (29 mg, 0.77 mmol). After being stirred for 15 min, the reaction was quenched by adding IR-120B resin (H^+ form). The insoluble materials were removed by filtration and the filtrate was concentrated to give a residue, which was chromatographed on a column of silica gel (8 g) with ethyl acetate-toluene (1:1) as eluant to give 404 mg (81 % from **9**) of compound **11** as a colorless syrup. ^1H NMR analysis showed **11** was a mixture consisting of α- and β-anomers in a ratio of 9:1. $[\alpha]_D^{25}$ + 31° (*c* 0.8, $CHCl_3$); IR (neat) 3400 cm^{-1}; ^1H and ^{13}C NMR data of the major isomer (α-anomer) are given in Table 1.

Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 51.34; H, 7.53.

1,2,3,6-Tetra-*O*-acetyl-5-*O*-methyl-α-L-talofuranose (12a) and its β-Anomer (12b). A solution of compound **11** (30 mg, 0.128 mmol) in tetrahydrofuran (1 mL) and 1 mol dm^{-3} aqueous sulfuric acid (0.5 mL) was heated at 50 °C for 7 h. The reaction mixture was neutralized with solid sodium hydrogencarbonate and concentrated to give a residue, which was dissolved in acetic anhydride (1 mL) and pyridine (1 mL). After being stirred at room temperature for 1 h, the mixture was concentrated then diluted with ethyl acetate. The resulting solution was washed successively with 1 mol dm^{-3} aqueous HCl solution, saturated sodium hydrogencarbonate solution and brine, then dried. Evaporation of the solvent left a syrup, which was chromatographed on a column of silica gel (3 g) with ethyl acetate-toluene (1:4) as eluant to give 11 mg (24%) of compound **12a** as a colorless syrup: $[\alpha]_D^{24}$ -19 ° (*c* 2.5, $CHCl_3$); IR (neat) 1750 cm^{-1}; ^1H and ^{13}C NMR data are given in Table 1.

Anal. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.76; H, 5.94.

Further elution gave 26 mg (56%) of a mixture of **12a** and **12b** (1.8:1) as a colorless syrup. ^1H NMR for **12b**: δ 6.43 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), other protons could not be characterized due to the overlap of the signals with those of the major isomer.

1L-3,4:5,6-Di-*O*-isopropylidene-1-*O*-(methylsulfonyl)-2-*O*-methyl-*chiro*-inositol (13). To a stirred solution of compound **3** (134 mg, 0.49 mmol) in pyridine (2 mL) was added methanesulfonyl chloride (0.068 mL, 0.88 mmol), and the mixture was stirred at room temperature for 3 h. The mixture was diluted with ethyl acetate and the resulting solution was washed successively with 0.5 mol dm^{-3} aqueous HCl solution, saturated sodium hydrogencarbonate solution and brine, then dried. Removal of the solvent gave analytically pure compound **13** as a crystalline residue (167 mg, 97%): mp 91-93 °C; $[\alpha]_D^{27}$ -14 ° (*c* 0.57, $CHCl_3$); IR (KBr) 1350 cm^{-1}; ^1H NMR (270 MHz) δ 1.37, 1.45, 1.52, 1.57 (4s, 12H, $2CMe_2$), 3.15 (s, 3H, SO_2Me), 3.58 (s, 3H, OMe), 3.64 (dd, 1H, $J_{3,4}$ = 6.8, $J_{4,5}$ = 7.8 Hz,

H-4), 3.66 (dd, 1H, $J_{2,3}$ = 8.8 Hz, H-3), 3.78 (dd, 1H, $J_{1,2}$ = 4.4 Hz, H-2), 4.39 (dd, 1H, $J_{5,6}$ = 5.9 Hz, H-5), 4.47 (dd, 1H, $J_{1,6}$ = 4.9 Hz, H-6), 5.19 (dd, 1H, H-1).

Anal. Calcd for $C_{14}H_{24}O_8S$: C, 47.72; H, 6.86. Found: C, 47.96; H, 6.70.

1L-(1,2,4/3)-1,2:3,4-Di-*O*-isopropylidene-1,2,3,4-tetrahydroxy-5-methoxy-5-cyclohexene (14). A mixture of compound **13** (47 mg, 0.13 mmol) and DBU (0.1 mL, 0.67 mmol) in toluene (1 mL) was heated under reflux for 108 h. The mixture was diluted with ethyl acetate and the resulting solution was washed with brine and dried. Evaporation of the solvent left a residue, which was purified on a column of silica gel (1.5 g) with ethyl acetate-toluene (1:10) as eluant to provide 20 mg (58%) of compound **14** as a crystalline residue: mp 61-63 °C; $[\alpha]_D^{20}$ -8 ° (*c* 0.50, $CHCl_3$); IR (KBr) 1645 cm^{-1}; ^1H NMR (90 MHz) δ 1.40, 1.47, 1.50, 1.53 (4s, 12H, $2CMe_2$), 3.68 (s, 3H, OMe), 3.82 (dd, 1H, $J_{2,3} = J_{3,4}$ = 9.0 Hz, H-3), 4.11 (m, 1H, H-4), 4.35 (dd, 1H, $J_{1,2}$ = 7.0 Hz, H-2), 4.67 (dd, 1H, $J_{1,6}$ = 3.5, $J_{4,6}$ = 2.0 Hz, H-6), 4.94 (dd, 1H, H-1).

Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.69; H, 7.64.

Methyl 2,3:4,5-Di-*O*-isopropylidene-L-guluronate (15). Ozone was bubbled through a solution of compound **14** (195 mg, 0.761 mmol) in dichloromethane (3 mL) at -78 °C for 30 min. After N_2 had been bubbled through the solution at -78 °C for 5 min, dimethyl sulfide (1.1 mL, 15 mmol) was added. The resultant mixture was stirred at room temperature for 4 h. The mixture was concentrated, then diluted with ethyl acetate. The resulting solution was washed with brine and dried. Evaporation of the solvent gave a residue, which was purified on a column of silica gel (6 g) with ethyl acetate-toluene (1:5) as eluant to afford 189 mg (86%) of compound **15** as a colorless syrup: $[\alpha]_D^{23}$ -82 ° (*c* 0.64, $CHCl_3$); IR (neat) 1755, 1740 cm^{-1}; ^1H and ^{13}C NMR data are given in Table 1.

Anal. Calcd for $C_{13}H_{20}O_7$: C, 54.16; H, 6.99. Found: C, 53.87; H, 6.66.

2,3,6-Tri-*O*-acetyl-5-*O*-formyl-L-mannono-1,4-lactone (16). To a stirred solution of chromium trioxide (1.33 g, 13.3 mmol) in acetic acid (20 mL) at room temperature was added a solution of compound **6a** (802 mg, 2.21 mmol) in acetic acid (10 mL) dropwise over 20 min. This mixture was stirred at 50 °C overnight. The mixture was diluted with chloroform and the resulting mixture was washed with saturated sodium hydrogencarbonate solution and brine, then dried. Evaporation of the solvent left a solid, which was recrystallized from ethanol to give 638 mg (87%) of compound **16** as white crystals: mp 126-127 °C; $[\alpha]_D^{22}$ -56 ° (*c* 1.0, $CHCl_3$); IR (KBr) 1770, 1750, 1710 cm^{-1}; ^1H NMR (400 MHz) δ 2.10, 2.12, 2.15 (3s, 9H, 3OAc), 4.21 (dd, 1H, $J_{5,6}$ = 4.4, $J_{6,6'}$ = 12.7 Hz, H-6), 4.66 (dd, 1H, $J_{5,6'}$ = 2.0 Hz, H-6'), 4.78 (ddd, 1H, $J_{3,4} = J_{4,CHO}$ = 1.5, $J_{4,5}$ = 9.3 Hz, H-4), 5.53 (dddd, 1H, $J_{5,CHO}$ = 1.0 Hz, H-5), 5.72 (m 2H, H-2,3), 7.98 (bs, 1H, CHO).

Anal. Calcd for $C_{13}H_{16}O_{10}$: C, 46.99; H, 4.85. Found: C, 47.10; H, 4.72.

Methyl 2,3,4,6-Tetra-*O*-acetyl-α-L-mannopyranoside (17). To a stirred solution of compound **16** (294 mg, 0.885 mmol) in tetrahydrofuran (13 mL) at -78 °C under argon was added 1.5 mol dm^{-3} solution of diisobutylaluminum hydride in toluene (4.2 mL, 6.3 mmol). After being stirred at -78°C for 4.5 h, the reaction was quenched by adding 1mol dm^{-3} HCl (11.2 mL). The resulting mixture was concentrated to give a residue. This residue was dissolved in 5% (weight) HCl in methanol (26 mL) and heated under reflux for 12 h. The reaction mixture was neutralized with basic lead(II) carbonate and the insoluble matter was removed by filtration through celite. Evaporation of the filtrate gave a residue, which was treated with acetic anhydride (5 mL) and pyridine (5 mL). After being stirred at room temperature for 5 h, the mixture was concentrated then diluted with ethyl acetate. The organic layer was washed successively with 1 mol dm^{-3} HCl solution, saturated sodium hydrogencarbonate solution and brine, and dried. Removal of the solvent gave a syrup, which was chromatographed on a column of silica gel (10 g) with ethyl acetate-toluene (1:12) as eluant to afford 122 mg (38%) of compound **17** as a colorless syrup; $[\alpha]_D^{21}$ -34 ° (*c* 0.9, $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR (400 MHz) δ 1.99, 2.04, 2.11, 2.16 (4s, 12H, 4OAc), 3.41 (s, 3H, OMe), 3.97 (ddd, 1H, $J_{4,5}$ = 9.8, $J_{5,6}$ = 2.4, $J_{5,6'}$ = 5.4 Hz, H-5), 4.12 (dd, 1H, $J_{6,6'}$ = 12.2 Hz, H-6), 4.29 (dd, 1H, H-6'), 4.72 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 5.24 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 5.28 (dd, 1H, $J_{3,4}$ = 9.8 Hz, H-4), 5.34 (dd, 1H, H-3). The IR and ^1H NMR spectra of **17** were superimposable on those of methyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside.[10]

1,2,3,4,5,6-Hexa-*O*-acetyl-D-glucitol (19). To a stirred suspension of lithium aluminum hydride (47 mg, 1.24 mmol) in ether (2 mL) at 0 °C was added a etheral solution (1 mL) of compound **15** (71 mg, 0.247 mmol). After being stirred at 0 °C for 4 h, the reaction was quenched by adding water, and the insoluble matter was removed by filtration through celite. Evaporation of the filtrate afforded a syrup, which was dissolved in methanol (2 mL). *p*-Toluenesulfonic acid (5 mg) was added to this solution and the mixture was stirred at room temperature for 11 h. The reaction mixture was neutralized with pyridine and then concentrated. The syrup obtained was treated with acetic anhydride (2 mL) and pyridine (2 mL) at room temperature for 3 h. The mixture was diluted with ethyl acetate. The resulting solution was washed with 1 mol dm^{-3} HCl solution, saturated sodium hydrogencarbonate solution and brine, then dried. Evaporation of the solvent left a residue, which was purified on a column of silica gel (5 g) with ethyl acetate-toluene (1:5) as eluant to provide 66 mg (61% overall yield) of compound **19** as a crystalline residue: mp 98-99 °C (from ethanol); $[\alpha]_D^{23}$ + 5 ° (*c* 0.44, acetone); IR (KBr) 1745 cm^{-1}; ^1H NMR (270 MHz) δ 2.06, 2.07, 2.08, 2.08, 2.09, 2.14 (6s, 18H, 6OAc), 4.02 (dd, 1H, J = 12.2, 5.9 Hz), 4.13 (dd, 1H, J = 12.2, 4.9 Hz), 4.26 (dd, 1H, J= 12.2, 3.4 Hz),

4.36 (dd, 1H, J = 12.2, 3.9 Hz), 5.05 (m, 1H), 5.25 (m, 1H), 5.43 (m, 2H). The IR and ^{1}H NMR spectra of **19** were superimposable on those of the authentic compound.[12]

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REFERENCES AND FOOTNOTES

1. a) J. van Alphen, *Ind. Eng. Chem.*, **43**, 141 (1951). b) N. Chida, M. Suzuki, M. Suwama, and S. Ogawa, *J. Carbohydr. Chem.*, **8**, 319 (1989).

2. S. Ogawa and A. Isaka, *Carbohydr. Res.*, **210**, 105 (1991).

3. a) H. Paulsen and F. R. Heiker, *Liebigs Ann. Chem.*, 2180 (1981). b) H. Paulsen and W. von Deyn, *Ibid.*, 133 (1987).

4. T. Akiyama, N. Takechi, and S. Ozaki, *Tetrahedron Lett.*, **31**, 1433 (1990).

5. A. P. Kozikowski, A. H. Fauq, G. Powis, and D. C. Meilder, *J. Am. Chem. Soc.*, **112**, 4528 (1990).

6. a) N. Chida, T. Tobe, M. Suwama, M. Ohtsuka, and S. Ogawa, *J. Chem. Soc., Chem. Commun.*, 994 (1990). b) N. Chida, T. Tobe, and S. Ogawa, *Tetrahedron Lett.*, **32**, 1063 (1991). c) N. Chida, K. Yamada, and S. Ogawa, *J. Chem. Soc., Chem. Commun.*, 588 (1991).

7. It has been reported that in the ^{1}H NMR spectra of acylated aldofuranoses, the coupling constant for *cis* hydrogens is in the range of 4.3 to 6.8 Hz and that less than 4 Hz may be ascribed to neighboring *trans* hydrogens. The chemical shifts of the anomeric protons which have *cis* relationship for neighboring hydrogens are observed at lower field than those which have *trans* relationship: see J. D. Stevens and H. G. Fletcher, Jr., *J. Org. Chem.*, **33**, 1799 (1968) and references therein. In addition, the reported coupling constants between H-1 and H-2 of 2,3:5,6-di-*O*-isopropylidene-α-D-mannose and 2,3:5,6-di-*O*-isopropylidene-β-D-allose (compounds whose structures are closely related to compound **5** and the major isomer of **11**, respectively) are both less than 0.1 Hz.[8] This fact also supported the assigned anomeric configurations of compound **5** and **11**.

8. P. Dais and A. S. Perlin, *Carbohydr. Res.*, **146**, 177 (1986).

9. S. J. Angyal and K. James, *Carbohydr. Res.*, **12**, 147 (1970).

10. The authentic sample was prepared from commercially available methyl α-D-mannopyranoside by conventional acetylation. It showed $[\alpha]_D^{24}$ + 36° (*c* 1.0, $CHCl_3$), lit[11] $[\alpha]_D$ + 49° ($CHCl_3$).

11. L. Hough and A. C. Richardson in *Rodd's Chemistry of Carbon Compounds*, Vol. IF; S. Coffey, Eds.; Elsevier Publishing: Amsterdam, 1967, p.240.

12. Authentic 1,2,3,4,5,6-hexa-*O*-acetyl-D-glucitol was prepared from commercially available D-glucitol by acetylation: mp 98-99 °C (from ethanol); $[\alpha]_D^{23}$ + 6 ° (*c* 0.49, acetone), lit[13] mp 99 °C; $[\alpha]_D^{20}$ + 10 ° (*c* 0.22, $CHCl_3$).

13. E. Pacsu and F. V. Rich, *J. Am. Chem. Soc.*, **55**, 3018 (1933).

14. Compound **5** has been utilized as a chiral starting material for the total synthesis of a novel sponge-derived natural product, bengamide E (see Ref. 6b).