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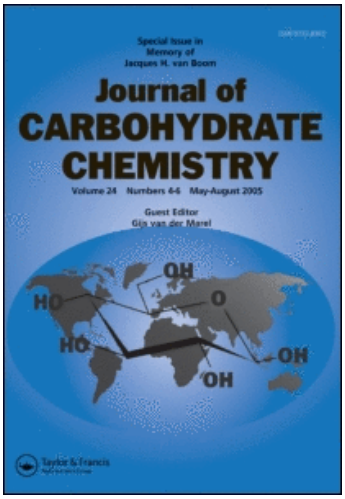

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Synthesis of Methyl 2,6-Dideoxy-3-C-Methyl-α-D-ribo- hexopyranoside (Methyl α-D-Mycaroside), a Component of the Antitomor Agent Mithramycin

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J. CARBOHYDRATE CHEMISTRY, 4(2), 227-242 (1985)

SYNTHESIS OF METHYL 2,6-DIDEOXY-3-C-METHYL-α-D-RIBO-HEXOPYRANOSIDE (METHYL α-D-MYCAROSIDE), A COMPONENT OF THE ANTITUMOR AGENT MITHRAMYCIN

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ABSTRACT

Methyl α-D-mannopyranoside (4) was converted into methyl 2,6-dideoxy-3-C-methyl-α-D-ribo-hexopyranoside (20) (methyl α-D-mycaroside) by an efficient sequence of reactions (Schemes 1 and 3). A similar set of reactions also was used to convert L-rhamnose (7) into methyl α-L-mycaroside (21). Attempted synthesis of methyl 2,6-dideoxy-3-C-methyl-α-D-arabino-hexopyranoside (22) (methyl α-D-olivomycoside) from methyl 6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-2-O-triflyl-α-D-arabino-hexopyranoside (18), a compound generated during synthesis of 20, was thwarted by a methyl migration which produced methyl 2,6-dideoxy-2-C-methyl-α-D-ribo-hexopyranoside (23).

INTRODUCTION

D-Mycarose (1), 2,6-dideoxy-3-C-methyl-D-ribo-hexose, is a branched-chain monosaccharide found in the antitumor agent mithramycin (2). Although mithramycin (2) is a valuable anticancer agent, its application is limited by the breadth of its antitumor spectrum and by its high toxicity.[1] Clinical and animal studies[2] as well as DNA binding site experiments[3] indicate that carbohydrate structure plays an essential role in the biological action of mithramycin (2); consequently, carbohydrate modified mithramycin analogs may

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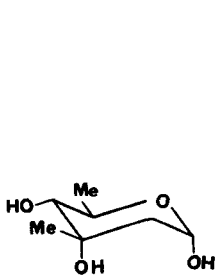

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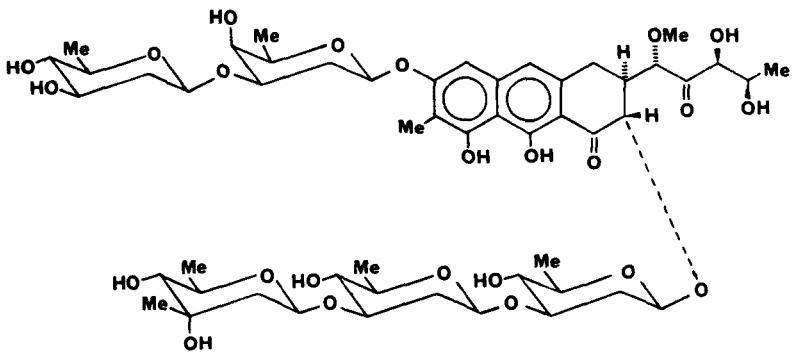

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be more effective than the parent compound (2) or less toxic or both. In order to test this proposal, a source of mithramycin analogs is needed. The best possibility, at present, for obtaining these analogs is by chemical synthesis.

One approach to the synthesis of mithramycin (2) and its carbohydrate modified analogs consists of constructing the di- and trisaccharide portions of the molecule prior to their attachment to the aglycone. Such an approach calls for a readily available source of a D-mycarose derivative suitable for use in trisaccharide construction. If the synthesis of this D-mycarose derivative were sufficiently flexible to allow simple structural change (e.g., inversion of configuration at a selected chiral center or replacement of a hydroxyl group by fluorine), then monosaccharides structurally related to D-mycarose (1), could be synthesized and incorporated into a trisaccharide unit. In this paper a reaction sequence for generating an appropriate D-mycarose derivative is described. This synthesis has the flexibility to permit formation of branched-chain sugars structurally related to compound 1.

D-Mycarose derivatives have been synthesized in the past by several different methods. Early work involved achiral starting materials and, consequently, produced a D,L-mixture.[4] The first synthesis of the pure D-isomer from a chiral starting material began with methyl 2-deoxy-α-D-*arabino*-hexopyranoside.[5] More recently, two additional syntheses, each with its own attractive features, have been reported.[6,7] None of the existing synthetic schemes, however, possessed the opportunity needed for alteration of the D-mycarose structure; therefore, the synthesis described below was developed. A useful feature of this synthesis is that it is easily adapted to generate L-mycarose derivatives also.

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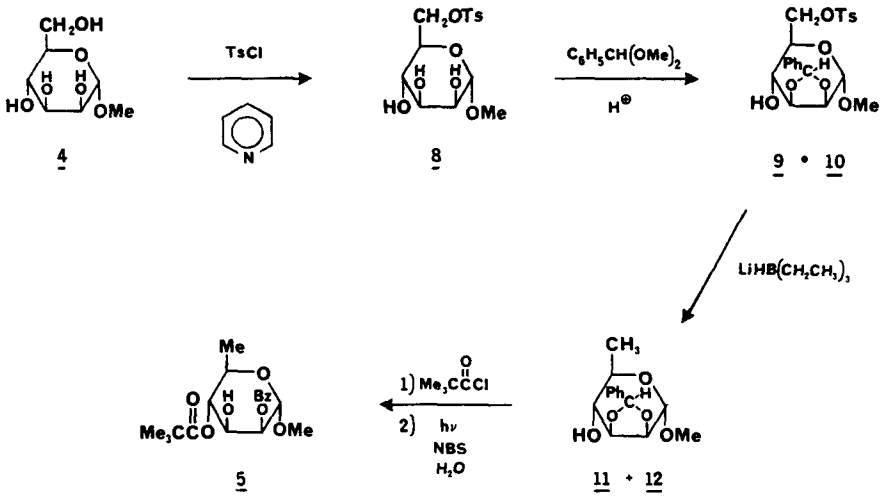
RESULTS AND DISCUSSION

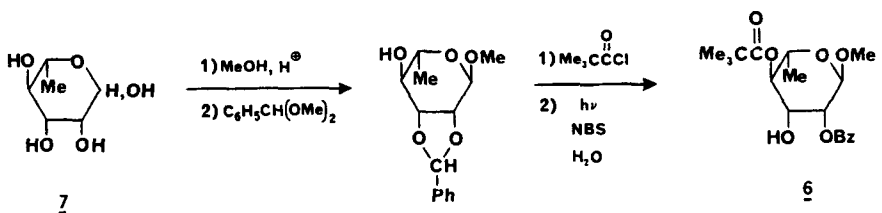
The first objective of this study was to convert methyl α-D-mannopyranoside (4) into methyl 2-O-benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-D-mannopyranoside (5) (Scheme 1). One reason compound 5 was selected as a target molecule was that its enantiomer (6) previously had been synthesized (in 60% overall yield, Scheme 2) from 6-deoxy-L-mannose (7, L-rhamnose);[8] therefore, once compounds 5 and 6 had been obtained, synthesis of enantiomerically pure D- or L-mycarose derivatives would follow the same pathway. Also, since L-rhamnose (7) and methyl α-D-mannopyranoside (4) are commercially available inexpensive compounds, they represent excellent starting materials for the synthesis of D- and L-mycarose derivatives.

The synthesis of compound 5 began with the reaction of methyl α-D-mannopyranoside (4) and tosyl chloride at -20 °C to give methyl 6-O-tosyl-α-D-mannopyranoside (8). When 8 was treated with α,α-dimethoxytoluene according to the Evans procedure,[9] it was converted into an inseparable mixture of methyl 2,3-O-benzylidene-(R and S)-6-O-tosyl-α-D-mannopyranosides (9 and 10).

Scheme 1



Scheme 2



This mixture (9 and 10) reacted with lithium triethylborohydride (LTBH), according to a method recently developed by Baer and Hanna,[10] to give the desired deoxy sugars 11 and 12. Although these compounds were separable, further reaction of individual compounds offered no advantage over reaction of the mixture itself. Esterification of the mixture (11 and 12) with pivaloyl chloride followed by irradiation in the presence of N-bromosuccinimide and water gave compound 5 in 40% overall yield from methyl α-D-mannopyranoside (4). Ring-opening of benzylidene acetals such as 11 and 12 under these conditions has been found to be regioselect-

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ive.[8] The favored conformer of the product has the benzoyloxy group axial and the hydroxy group equatorial.

Two methods were used for the oxidation of compound 5. The first of these involved esterification with pyruvoyl chloride followed by irradiation of the pyruvate ester to give methyl 2-O-benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-D-arabino-hexopyranosid-3-ulose (13) in 73% yield (Scheme 3). A second method consisted of reaction of 5 with pyridinium chlorochromate in the presence of molecular sieve. The pyridinium chlorochromate oxidation took place in higher yield (87%) than pyruvate photolysis and was considerably faster for conversion of large quantities of material. The primary disadvantages to chromate oxidation were that chromatography was necessary to remove the black, tarry chromium salts which formed and that epimerization at C-2 in the oxidation product 13 took place. The epimerization process was suppressed by the addition of sodium acetate to the reaction mixture prior to introduction of the oxidizing agent.

Reaction of methyl magnesium iodide with the carbonyl compound 13 introduced the methyl branch at C-3 and also removed benzoyl groups from some molecules. Since deprotection of O-2 was the next step in the sequence, complete removal of the benzoyl group was accomplished by dissolving the product mixture from the Grignard reaction in methanol and adding a strongly basic ion exchange resin. The pivaloyl group was unaffected by these reaction conditions; in fact, this protecting group was chosen so that regioselective debenzoylation could be accomplished at this stage in the synthesis. Some of the major product from the deprotection process crystallized from the reaction mixture. Chromatography of the residue yielded more of the major product (67% total yield) and a minor product (10%). The NMR spectra of these compounds (Tables 1 and 2) indicated that they were the C-3 epimers 15 and 16; however, without further

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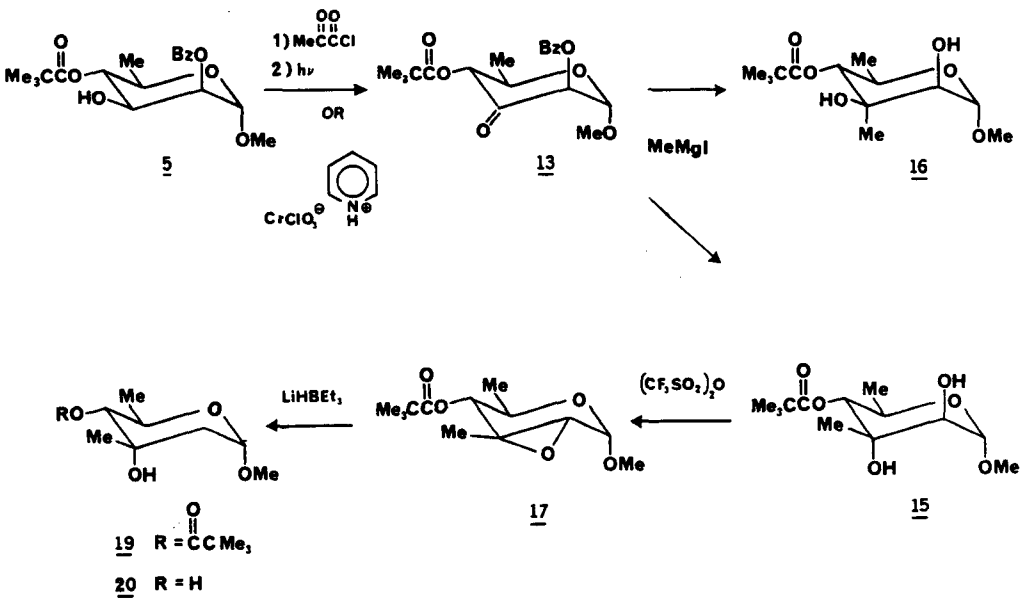
Scheme 3



information it could not be determined which of these two was the major product.

Treatment of the major product (from the Grignard reaction) with triflic anhydride at room temperature resulted in rapid, quantitative formation of methyl 2,3-anhydro-6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-allopyranoside (17). This procedure represents a mild method for epoxide formation. Epoxide formation in this case established 15 as the major product from the Grignard reaction since only 15 (and not 16) was capable of three-membered ring formation under these conditions. Reaction of 16 with triflic anhydride produced the expected 2-O-triflyl compound 18 (Scheme 4).

Reaction of the anhydro sugar 17 with an equal molar amount of lithium triethylborohydride (LTBH) opened the epoxide ring to give the partially protected D-mycarose derivative 19, the compound desired for future use in the mithramycin trisaccharide synthesis. (Treatment of 17 with other nucleophiles should allow formation of a

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Table 1. ^{1}H NMR Spectral Data[a]

Compound	H_1	H_2	H_3	H_4	H_5	H_6	OMe	CMe_3	Additional Absorptions
5	4.79 $J_{1,2}$=1.6	5.32 $J_{2,3}$=3.5	4.13 $J_{3,4}$=9.8	5.03 $J_{4,5}$=9.6	3.87 $J_{5,6}$=6.0	1.24	3.39	1.24	8.17-7.93(C_6H_5) 7.60-7.13(C_6H_5)
13	5.10 $J_{1,2}$=1.7	5.23	-	5.33 $J_{4,5}$=9.9	4.18 $J_{5,6}$=6.2	1.41	3.44	1.27	
15	4.72 $J_{1,2}$=0.3	3.55	-	4.90 $J_{4,5}$=10.1	3.98 $J_{5,6}$=6.3	1.17	3.45	1.25	1.17 (C_3-Me)
16	4.75 $J_{1,2}$=1.4	3.55	-	4.73 $J_{4,5}$=9.8	3.82 $J_{5,6}$=6.2	1.17	3.38	1.24	1.28(C_3-Me)
17	4.85 $J_{1,2}$=3.1	3.30	-	4.96 $J_{4,5}$=9.4	3.86 $J_{5,6}$=6.3	1.08	3.44	1.25	1.31(C_3-Me)
18	4.81 $J_{1,2}$=0.3	4.68	-	4.74 $J_{4,5}$=9.9	3.79 $J_{5,6}$=6.1	1.24	3.41	1.23	1.39(C_3-Me)
19	4.78 $J_{1,2}$=1.8 $J_{1,2}$=3.5	1.94 1.91	-	4.61 $J_{4,5}$=10.1	4.04 $J_{5,6}$=6.0	1.23	3.38	1.25	1.09(C_3-Me)
20	4.75 $J_{1,2a}$=1.4 $J_{1,2e}$=3.4	2.03 1.80 $J_{2,2'}$=14.6	- $J_{4,5}$=9.7	2.94 $J_{5,6}$=9.7	3.60 $J_{5,6}$=6.2	1.34	3.37	-	1.22(C_3-Me)
23	4.52 $J_{1,2}$=3.0	1.88 $J_{2,Me}$=7.2 $J_{2,3}$=3.0	3.70 $J_{3,4}$=4.3	3.10 $J_{4,5}$=9.9	3.57 $J_{5,6}$=6.2	1.33	3.37	-	1.11(C_2-Me)

a. Chemical shifts are relative to Me_4Si (0 ppm). Coupling constants are in Hertz.

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Table 2. ^{13}C NMR Spectral Data[a]

	5[c]	13[d]	15	16	17	18[e]	19	20	23
C_1	98.60	100.21	101.64	101.09	94.44	98.41	98.42	98.20	101.71
C_2	74.79[b]	76.62[b]	73.47[b]	72.47	60.79	88.09	41.39	40.59	37.43
C_3	69.06	194.54	72.33	74.84	57.37	71.27	69.67	69.70	71.81[b]
C_4	73.38[b]	76.42[b]	73.13[b]	76.77[b]	73.66	75.85	76.59	76.26	73.10[b]
C_5	66.13	68.69	62.98	65.16	63.13	65.39	62.67	65.22	63.43
C_6	17.53	18.34	17.11	17.45	17.93	17.35	17.23	17.71	17.32
OMe	55.20	55.22	55.31	55.04	55.29	55.57	54.92	54.73	55.08
$Me_3\underline{C}$	39.01	38.66	38.89	38.96	38.76	38.96	38.94	-	-
$\underline{Me}_3C$	27.12	26.89	27.01	27.01	26.89	26.89	27.08	-	
R $\underline{C}$=O	179.03	176.79	177.85	178.91	177.69	179.11	177.83	-	-
C_3-$\underline{Me}$	-	-	22.05	19.19	16.88	19.22	25.62	25.47	12.26

a. Chemical shifts are relative to Me_4Si (0 ppm).
b. Assignments for a particular compound interchanged.
c. Additional absorptions at 166.39, 129.68, 129.93, 128.53, and 133.39 ppm.
d. Additional absorptions at 164.63, 135.93, 133.58, 129.84, and 128.41 ppm.
e. Additional absorption at 118.36 (CF_3) ppm.

variety of 2-substituted compounds related to D-mycarose.) Reaction of 17 with excess lithium triethylborohydride opened the epoxide ring and removed the pivaloyl group to give methyl α-D-mycaroside 20 in 96% yield. This reaction confirmed the stereochemical assignment made to compound 15. The overall yield of methyl α-D-mycaroside (20) from methyl α-D-mannopyranoside (4) was 22%.

Methyl α-L-mycaroside (21), the enantiomer of 20, also was synthesized. This synthesis began with the previously reported conversion of L-rhamnose (7) into methyl 2-O-benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-L-mannopyranoside (6).[8] It was completed by conducting the sequence of reactions shown in Scheme 3 using compound 6, the enantiomer of 5, as the starting material. The L-rhamnose (7) to methyl α-L-mycaroside (21) transformation took place in 31% overall yield.

The final experiment conducted involved the triflate 18. Treatment of sulfonates, such as compounds 9 and 10, with lithium triethylborohydride (LTBH) produces in some cases the corresponding deoxy sugars.[11] The possiblity existed, therefore, that treatment of the 2-O-triflyl compound 18 with LTBH would produce methyl 2,6-dideoxy-3-C-methyl-α-D-arabino-hexopyranoside (22) (methyl α-D-olivomycoside), the C-3 epimer of 20. When 18 was treated with LTBH, a 2,6-dideoxy sugar was formed; however, rather than the expected product 22, the rearranged methyl 2,6-dideoxy-2-C-methyl-α-D-ribo-hexopyranoside (23) was produced. A proposed mechanism for this rearrangement is shown in Scheme 4.

EXPERIMENTAL

General Information. ^{1}H and ^{13}C NMR spectra were obtained from a Varian FT-80A spectrometer. Preparative liquid chromatography was conducted using a Waters Prep LC/SYSTEM 500A. Mass spectra were determined

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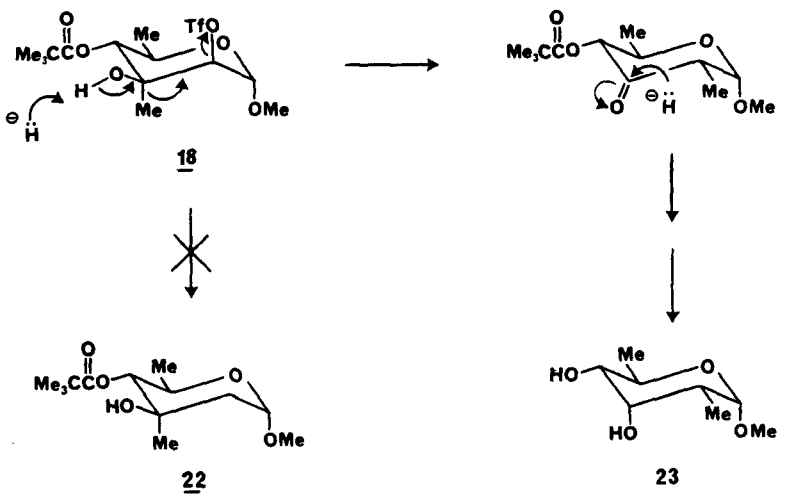
Scheme 4



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with a Finnigan 1015-D spectrometer with methane as a reagent gas and an ionizing voltage of 150 eV.

Synthesis of Methyl 3,4-O-Benzylidene-(S and R)-6-deoxy-α-D-mannopyranosides (11 and 12). The procedure described here for introduction of the benzylidene group is a modification of that used by Evans[9] to synthesize methyl 4,6-O-benzylidene-α-D-glucopyranoside. Methyl 6-O-tosyl-α-D-mannopyranoside[12] (4) (36 g, 0.10 mol) and 16.7 g (16.5 mL, 0.11 mol) of α,α-dimethoxytoluene were dissolved in 200 mL of N,N-dimethylformamide (DMF) containing 0.5 g of p-toluenesulfonic acid monohydrate. The flask was attached to a rotary evaporator and evacuated while being heated. When the temperature reached 90 °C, much of the DMF and other volatile material had distilled. Pyridine (2 mL) was added and the reaction mixture was placed under vacuum using a mechanical pump and held at 50 °C until all volatile materials had been removed. The portion of the residue which was soluble in ethyl ether was separated and the ether was distilled to give 36.9 g of material. The ^{1}H and ^{13}C NMR spectra of this material indicated it to be a mixture of benzyli-

dene acetals; however, since these compounds could not be separated by chromatography, they were used directly in the next reaction.

The procedure described in this paragraph for formation of the 6-deoxy compounds 11 and 12 is essentially that used by Baer and Hanna.[13] The mixture of benzylidene acetals (36.9 g) was dissolved in 150 mL of tetrahydrofuran and the reaction flask was purged with nitrogen while 300 mL of a 1.0 M solution of lithium triethylborohydride[14] (LTBH) in tetrahydrofuran was added in a dropwise manner. The reaction mixture was refluxed for 30 min and then allowed to cool to room temperature. The excess hydride reagent was destroyed by dropwise addition of 20 mL of methanol. The reaction mixture was poured into 400 mL of ice-water and 100 mL of 30% H_2O_2 was added slowly with stirring and cooling. The stirring was continued for 2 h and then the reaction mixture was extracted with three 300 mL portions of CH_2Cl_2. The solvent was distilled to give 21.8 g (0.081 mol, 80% from 4) of a 1:1 mixture of methyl 3,4-O-benzylidene-(S and R)-6-deoxy-α-D-mannopyranoside (11 and 12). A 0.5 g sample of this mixture was chromatographed on a 2.5 x 20 cm column of 240-400 mesh silica gel using 1:10 ethyl acetate-toluene to give pure samples of 11 and 12. These compounds (11 and 12) were identical in ^{13}C and ^{1}H NMR spectra to those prepared independently by the benzylidenation of methyl 6-deoxy-α-D-mannopyranoside.[15]

Synthesis of Methyl 2-O-Benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-D-mannopyranoside (5). The esterification of the mixture of 11 and 12 and the reaction of these esters with N-bromosuccinimide and water to give 5 was conducted according to the procedure used to prepare 6,[8] the enantiomer of 5. The ^{1}H and ^{13}C NMR spectra for 5 are given in Tables 1 and 2, respectively, and are identical to those previously reported[8] for 6.

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Synthesis of Methyl 2-O-Benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-D-arabino-hexopyranosid-3-ulose (13).

Procedure A. Compound 5 (44 g, 0.12 mol) was dissolved in 300 mL of dry CH_2Cl_2. To this stirred, cooled (20 °C) solution was added 10 g (0.12 mol) of sodium acetate and 54 g (.25 mol) of pyridinium chlorochromate. The reaction mixture became dark colored after a few min. After two h, the reaction mixture was filtered and the filtrate passed through a 5 x 20 cm column of silica gel by eluting with 1:1 ethyl ether-methylene chloride. This process removed the black material. Concentration of the reaction mixture under reduced pressure gave 38 g (0.10 mol, 87%) of methyl 2-O-benzoyl-6-deoxy-4-O-(2,2-dimethylpropanoyl)-α-D-arabino-hexopyranosid-3-ulose (13), which did not crystallize. Compound 13 was identified on the basis of its ^1H NMR (Table 1) and ^{13}C NMR (Table 2) spectra. Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.62; H, 6.64. Found: C, 62.41; H, 6.62.

Procedure B. Compound 5 (2.53 g, 0.69 x 10^{-2} mmol) was dissolved in 50 mL of CH_2Cl_2 containing 5 mL of pyridine. Pyruvoyl chloride (1.5 mL) in 10 mL of CH_2Cl_2 was added to the rapidly stirred, cooled (ice-bath) sugar solution. After addition was complete, the reaction mixture was allowed to stand for 3 h at room temperature and then 200 mL of hexane was added slowly. This solution was filtered to remove the precipitated material. The solvent was distilled from the filtrate to leave a yellow residue. This residue was extracted with two 250 mL portions of hexane. The hexane was distilled to leave a pale yellow syrup which was dissolved in 500 mL of benzene. This solution was purged with N_2 for 1 h and then irradiated for 5 h. The benzene was distilled and the residue (brown) was extracted with two 100 mL portions of hexane. The hexane was distilled to give 1.83 g (0.50 x 10^{-2} mol, 73%) of compound 13.

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Synthesis of Methyl 6-Deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-altropyranoside (15) and Methyl 6-Deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-mannopyranoside (16). Compound 13 (38 g, 0.10 mol) was dissolved in 500 mL of anhydrous ethyl ether and 50 mL of a 3.0 M solution of methyl magnesium iodide[14] was added at such a rate that the solvent gently refluxed. After the Grignard addition was complete, the reaction mixture stood for 2 h and then 200 mL of H_2O was added (slowly at first). Dilute (5%) hydrochloric acid was added with stirring until the precipitate just dissolved. (The solution was still basic.) The phases were separated and the aqueous phase was washed with an equal volume of ethyl ether. The organic extracts were combined and passed through a 5 x 20 cm column of silica gel. The ether was evaporated and the residue was dissolved in 200 mL of methanol containing 50 g of Baker ANGA-542 ion exchange resin (strong base) and stirred for 2 h. The solution was filtered and the solvent distilled. The residue was dissolved in the minimum amount of 1:1 ethyl acetate-toluene and allowed to stand until crystallization was complete. This produced 15.4 g (5.57×10^{-2} mol) of 6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-altropyranoside (15), mp 140-142 °C. Anal. Calcd for $C_{13}H_{24}O_6$: C, 56.50; H, 8.75. Found: C, 56.69; H, 8.86. The ^1H and ^{13}C NMR spectra are in Tables 1 and 2, respectively.

The residue after crystallization was chromatographed using a Waters Prep LC/SYSTEM 500 A with 1:1 toluene-ethyl acetate as the solvent. This gave an additional 3.1 g of 15 and 2.7 g of methyl 6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-mannopyranoside (16), a compound which failed to crystallize. Anal. Calcd for $C_{13}H_{24}O_6$: C, 56.50; H, 8.75. Found: C, 56.69; H, 8.50. The ^1H and ^{13}C NMR spectra of 16 are found in Tables 1 and 2, respectively.

Synthesis of Methyl 2,3-Anhydro-6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-allopyranoside (17). Compound 15 (4.40 g, 1.59 x 10^{-2} mol) was dissolved in 50 mL of CH_2Cl_2 containing 5 mL of pyridine. This solution was cooled to -20 °C and 3.4 mL (5.7 g, 2.0 x 10^{-2} mol) of triflic anhydride was added dropwise with stirring. The reaction mixture warmed to room temperature over a period of 4 h. Tlc analysis showed that the starting material had reacted completely. Water (20 mL) was added and the stirring continued for 15 min. The layers were separated and the aqueous layer extracted with 50 mL of CH_2CL_2. The organic extracts were combined and the solvent evaporated under reduced pressure to give 3.9 g (1.5 x 10^{-2} mol, 94%) of methyl 2,3-anhydro-6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-allopyranoside (17), mp 52.5-54.0 °C. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.44; H, 8.59. Found: 60.15, H, 8.70. NMR spectra are given in Tables 1 and 2.

Synthesis of Methyl 2,6-Dideoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-α-D-ribo-hexopyranoside (19). Compound 17 (3.69 g, 1.50 x 10^{-2} mol) was dissolved in 50 mL of tetrahydrofuran (THF) under nitrogen and 20 mL of a 1 M solution of lithium triethylborohydride (LTBH) in THF was added slowly. After stirring for 15 min, 5 mL of methanol was added slowly. The reaction mixture was poured into 400 mL of ice-water and 10 mL of H_2O_2 was added with rapid stirring. After 15 min, the aqueous solution was extracted with $CHCl_3$ (3 x 200 mL). The solvent was distilled from the combined $CHCl_3$ extracts to give 3.7 g (1.5 x 10^{-2} mol) of compound 19, mp 73-75 °C. ^1H and ^{13}C NMR spectra are given in Tables 1 and 2, respectively. Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 59.91; H, 9.25.

Synthesis of Methyl 2,6-Dideoxy-3-C-methyl-α-D-ribo-hexopyranoside (20, methyl α-D-mycaroside). Compound 17 (18.1 g, 6.96 x 10^{-2} mol) was treated with LTBH in the same manner as was used for the synthesis of

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compounds 11 and 12 (the Baer and Hanna procedure[10]) to give 11.8 g (6.68×10^{-2} mol, 96%) of methyl α-D-mycaroside (20), mp 56-57.5 °C (lit.[6] 56-58 °C), identical in ^{1}H NMR spectrum with that reported in the literature.[16]

Synthesis of Methyl 2,6-Dideoxy-2-C-methyl-α-D-ribo-hexopyranoside (23). Compound 18 (1.1 g, 4.5×10^{-3} mol) was dissolved in 20 mL of CH_2Cl_2 containing 3 mL pyridine. The solution was cooled to -20 °C and 2.0 mL of triflic anhydride was added with stirring in a dropwise manner. The reaction mixture warmed to room temperature over a period of 2 h. Water (20 mL) was added and the stirring continued for 15 min. The layers were separated and the aqueous layer extracted with 50 mL of CH_2Cl_2. The organic extracts were combined and the solvent evaporated under reduced pressure. The residue then was stirred with 125 mL of hexane and the solution decanted from the residue. The hexane was evaporated under reduced pressure to give 1.8 g (4.4×10^{-3} mol) of methyl 6-deoxy-3-C-methyl-4-O-(2,2-dimethylpropanoyl)-2-O-triflyl-α-D-arabino-hexopyranoside (18), mp 114-115 °C. The ^{1}H and ^{13}C NMR spectra for 18 are given in Tables 1 and 2; however, this compound was unstable and generally was used immediately after preparation.

Compound 18 (1.8 g) was treated with LTBH in the same manner as was used for the synthesis of compounds 11 and 12 (the Baer and Hanna procedure[10]) to give 0.70 g (3.9×10^{-3} mol, 88%) of methyl 2,6-dideoxy-2-C-methyl-α-D-ribo-hexopyranoside (23), mp 110-112 °C. Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.29; H, 9.01. The ^{1}H and ^{13}C NMR spectra are given in Tables 1 and 2, respectively.

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