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SYNTHESIS OF L-NOGALOSE AND ITS ENANTIOMER*

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ABSTRACT

L-Nogalose (6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-L-mannopyranose) and its enantiomer were synthesized *via* (*a*) introduction of the *C*-methyl branch by successive epoxidation and reduction of methyl 3,6-dideoxy-2,4-di-*O*-methyl-3-*C*-methylene-α-L-*arabino*-hexopyranoside, and (*b*) deoxygenation at C-6 of methyl 4,6-*O*-benzylidene-3-*C*-methyl-2-*O*-methyl-α-D-mannopyranoside, and *O*-methylation of the product.

INTRODUCTION

L-Nogalose (**1**) is the component sugar of nogalamycin[2], an antibiotic highly active against Gram-positive bacteria and KB cells *in vivo*. The absolute configuration was established as 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-L-mannopyranose by Wiley and co-workers[3]. The enantiomeric structure of D-evalose (**2**), found in the oligosaccharide antibiotics everninomicin B (ref. 4) and flambamycin[5], was proved by conversion into D-nogalose[6]. Brimacombe and Rollins[7] synthesized D-nogalose through addition of methylmagnesium iodide to 1,2:5,6-di-*O*-isopropylidene-β-D-*arabino*-hexofuranos-3-ulose, but the synthesis of L-nogalose through configurational inversion of C-5 of 6-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-3-*O*-methyl-5-*O*-(methylsulfonyl)-α-D-gulofuranose was unsuccessful We now describe, in detail, the synthesis of **1** and its enantiomer through different pathways that were previously communicated[8,9]

RESULTS AND DISCUSSION

Formation of the 2,3-*O*-dibutylstannylene derivative (**8**) from methyl 4-*O*-methyl-α-L-rhamnopyranoside[10] (**3**) and dibutyltin oxide in methanol, and reaction with a slight excess of benzyl bromide in *N*,*N*-dimethylformamide for 20 min at 100° gave, almost exclusively, the corresponding 3-*O*-benzyl derivative (**4**) due to reaction at the equatorially oriented oxygen atom, as shown in the case of other axial–equatorial dibutylstannylene compounds[11]. Treatment of **4** with methyl iodide and sodium

*Branched-chain Sugars, Part XXVII. For Part XXVI, see ref. 1

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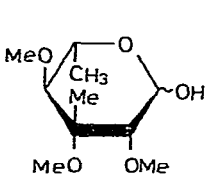
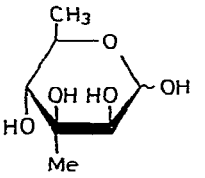
hydride in dimethyl sulfoxide gave the corresponding 2-*O*-methyl derivative (**5**) in 85% yield. Hydrogenation of **5** in 70% acetic acid in the presence of 10% palladium-on-carbon gave syrupy methyl 6-deoxy-2,4-di-*O*-methyl-α-L-mannopyranoside (**6**) in 74% yield. The structure of **6** was confirmed by the n.m.r. spectrum of the corresponding 3-*O*-acetyl derivative (**7**).



1



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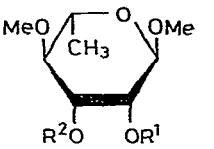
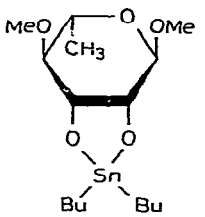


3 $R^1 = R^2 = H$
4 $R^1 = H$, $R^2 = PhCH_2$
5 $R^1 = Me$, $R^2 = PhCH_2$
6 $R^1 = Me$ $R^2 = H$
7 $R^1 = Me$, $R^2 = Ac$



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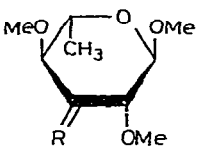
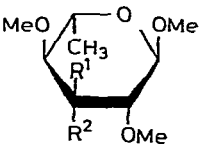
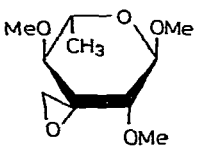


9 R = O
10 R = CH_2





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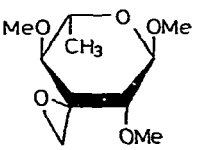


12

13 $R^1 = Me$, $R^2 = OH$
14 $R^1 = OH$, $R^2 = Me$
15 $R^1 = Me$, $R^2 = OMe$

Oxidation of **6** with ruthenium tetraoxide and aqueous sodium periodate in carbon tetrachloride in the presence of potassium carbonate gave methyl 6-deoxy-2,4-di-*O*-methyl-α-L-*arabino*-hexopyranosid-3-ulose (**9**) in good yield. Introduction of the 3-*C*-methyl group by reaction of **9** with methylmagnesium iodide gave mainly the epimer of undesired configuration* (**14**) in the ratio of 4 : 1, and attempted reaction with diazomethane gave a complex result[13]. Therefore, another pathway for epoxidation of the corresponding 3-*C*-methylene derivative[14] was examined. Compound **9**

*After our communication[8] had been published, Valente *et al.*[12] reported that the Grignard reaction of 6-deoxy-1,2-*O*-cyclohexylidene-4-*O*-methyl-β-L-*arabino*-hexopyranos-3-ulose, obtained from the allyl glycoside of **4**, gave predominantly the 3-*C*-methyl derivative having the desired configuration from which **1** was synthesized.

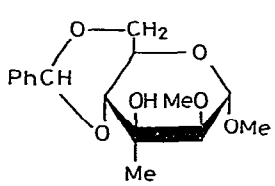
TABLE I

PHYSICAL CONSTANTS OF COMPOUND **15** AND ITS ENANTIOMER (**20**)

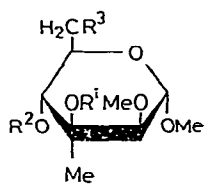
Compound	$[\alpha]_D$ *(in CH_3OH) (degrees)*	*M.p. (°C)*	*N.m.r. parameters*					
			H-1 ($J_{1,2}$)	*H-2*	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6*	*Other protons*
Synthetic **15**	−49.4	41–43	4.72 d (2.0)	3.37 d	3.07 d (9.5)	3.63 m (6.3)	1.28 d	1.31 (CMe), 3.53 (OMe) 3.49 (OMe), 3.36 (OMe) 3.27 (OMe)
Enantiomer **20**	+50	41–43	4.72 d (2.0)	3.37 d	3.07 d (9.5)	3.63 m (6.3)	1.28 d	1.31 (CMe), 3.53 (OMe) 3.49 (OMe), 3.36 (OMe) 3.27 (OMe)
Reported **15**	−48.4	41–43	4.72 d (2.0)		3.07 d (9.5)	3.63 m (6.3)	1.28 d	1.31 (CMe), 3.53 (OMe) 3.49 (OMe), 3.36 (OMe) 3.28 (OMe)

was converted into the 3-*C*-methylene derivative (**10**), in 66% yield, by the usual Wittig reaction. Oxidation of **10** with *m*-chloroperoxybenzoic acid in 1,2-dichloroethane at room temperature gave an epimeric mixture of the corresponding *spiro*-epoxides (**11** and **12**) in 65% yield. The ratio of **11** to **12** was estimated to be 1.1 from the n.m.r. spectrum, but only **11** could be isolated in pure state. The two isomers were readily separated after reduction of the mixture, with lithium aluminum hydride, to the corresponding 3-*C*-methyl derivatives (**13** and **14**). Treatment of methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-mannopyranoside (**13**) with sodium hydride and methyl iodide in dimethyl sulfoxide gave the corresponding 3-*O*-methyl derivative (**15**) in 85% yield; this was purified by sublimation at 40°/0.03 mm Hg, to give colorless crystals. The physical constants of **15** were in good agreement with those reported (see Table I). Hydrolysis of **15** with 0.5M sulfuric acid for 30 min at 90–95° gave, in 78% yield, L-nogalose (**1**) identical with that reported[2].

On the other hand, methyl 4,6-*O*-benzylidene-3-*C*-methyl-2-*O*-methyl-α-D-mannopyranoside (**16**), obtained by the epoxidation and reduction of the corre-



16



17 $R^1 = H$, $R^2 = Bz$, $R^3 = Br$

18 $R^1 = R^3 = H$, $R^2 = Bz$

19 $R^1 = R^2 = R^3 = H$

20 $R^1 = R^2 = Me$, $R^3 = H$

sponding 3-*C*-methylene derivative[15], was treated with *N*-bromosuccinimide in carbon tetrachloride, to give methyl 4-*O*-benzoyl-6-bromo-6-deoxy-3-*C*-methyl-2-*O*-methyl-α-D-mannopyranoside (**17**) in 65% yield. Reduction of **17** in benzene with tributylstannane, in the presence of α,α'-azobis(isobutanonitrile), gave the corresponding 6-deoxy derivative (**18**) in 81% yield. Treatment of **18** with methanolic ammonia afforded the corresponding *O*-debenzoylated product (**19**) in quantitative yield, and *O*-methylation of **19** by the usual method gave methyl 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-α-D-mannopyranoside (**20**: methyl D-nogaloside) in 88% yield. The physical constants of **20** were completely identical with those of **15** (see Table I), except for the reverse sign of the rotational value.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were evaporated under diminished pressure at a bath temperature not exceeding 50°. Specific rotations were measured with a Carl Zeiss LEP-Al polarimeter, using a 0.5-dm tube. I.r. spectra were recorded with a Hitachi Model EPI-G2 spectrometer. Mass spectra were recorded with a SHIMADSU-LKB 9000S instrument. N.m.r. spectra were recorded with a JEOL PS 100-MHz spectrometer with tetramethylsilane as the internal standard, for solutions in chloroform-*d*, unless stated otherwise.

Methyl 3-O-benzyl-6-deoxy-4-O-methyl-α-L-mannopyranoside (**4**). — Methyl 6-deoxy-4-*O*-methyl-α-L-mannopyranoside[10] (**3**; 19.6 g, 102 mmol) was boiled under reflux with dibutyltin oxide (25.4 g, 102 mmol) in dry methanol (100 mL) for 1 h (clear solution), and then the solution was cooled, and evaporated. The resulting methyl 2,3-*O*-dibutylstannylene-4-*O*-methyl-α-L-mannopyranoside (**8**) was dried *in vacuo*, dissolved in *N*,*N*-dimethylformamide (360 mL), and treated with benzyl bromide (24.4 g, 143 mmol). After the mixture had been heated for 1 h at 100°, disappearance of the starting material was ascertained by t.l.c. with 8:1 benzene–methanol. Evaporation of the solvent, and purification of the product on a column of silica gel, gave syrupy **4** (17.8 g, 62% yield), $[\alpha]_D^{26}$ −39.7° (*c* 1.0, methanol); n.m.r.: δ 7.33 (s, 5 H, Ph), 4.65 (s, 2 H, $PhCH_2$), 4.62 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 3.95 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 3.68 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.14 (dd, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.60 (oct, 1 H, $J_{5,6}$ 6.1 Hz, H-5), 1.29 (d, 3 H, H-6), 3.36 and 3.53 (each s, 6 H, 2 OMe), and 2.68 (s, 1 H, OH).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.53; H, 7.60.

Methyl 3-O-benzyl-6-deoxy-2,4-di-O-methyl-α-L-mannopyranoside (**5**). — To a suspension of sodium hydride (1.5 g, 64 mmol) in dimethyl sulfoxide (100 mL) was added, dropwise, a solution of **4** (12 g, 42 mmol) in dimethyl sulfoxide (100 mL). After the mixture had been stirred for 3 h at room temperature, methyl iodide (18 g, 126 mmol) was added dropwise, and the mixture was stirred for 2 h. The usual processing of the mixture, and purification of the product on a column of silica gel with 4:1 benzene–ethyl acetate, gave syrupy **5** (10.6 g, 85% yield), $[\alpha]_D^{17}$ −48.6° (*c* 1.0, carbon tetrachloride); n.m.r.: δ 7.33 (s, 5 H, Ph), 4.69 (s, 2 H, $PhCH_2$), 4.66

(d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 3.8–3.0 (m, 4 H, H-2,3,4,5), 3.32, 3 57, and 3.48 (each s, 9 H, 3 OMe), and 1.31 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6).

Anal. Calc. for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.42; H, 8.32.

*Methyl 6-deoxy-2,4-di-O-methyl-α-*L*-mannopyranoside* (**6**). — On catalytic hydrogenolysis of **5** (2.1 g, 7.1 mmol) in 70% acetic acid (100 mL) in the presence of 10% palladium-on-charcoal (3 g), t.l.c. did not show any starting material after 40 h, and then the usual processing of the mixture gave **6** (1.38 g, 94% yield), $[\alpha]_D^{17}$ −51.4° (*c* 1.0, carbon tetrachloride): n.m.r.: δ 4.72 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 3 45 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2), 3 56 (dd, 1 H, $J_{3,4}$ 9.8 Hz, H-3), 2.97 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.75 (oct, 1 H, $J_{5,6}$ 6.1 Hz, H-5), 3.36, 3.49, and 3.58 (each s, 9 H, 3 OMe), and 1.29 (d, 3 H, H-6).

Anal. Calc. for $C_9H_{18}O_5$: C, 52.41; H, 8.80. Found. C, 52.50; H, 8.77.

*Methyl 3-O-acetyl-6-deoxy-2,4-di-O-methyl-α-*L*-mannopyranoside* (**7**). — Acetylation of **6** (0.1 g, 0.49 mmol) with acetic anhydride in pyridine gave 7 (0.1 g, 85%), $[\alpha]_D^{25}$ −28.4° (*c* 1.0, methanol); n.m.r.: δ 5.08 (dd, 1 H, $J_{2,3}$ 3.5, $J_{3,4}$ 9.8 Hz, H-3), 4.60 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 3.67 (dd, 1 H, H-2), 3.14 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.74 (oct, 1 H, $J_{5,6}$ 6.1 Hz, H-5), 3.37, 3.40, and 3.44 (each s, 9 H, 3 OMe), 2.1 (*s*, 3 H, Ac), and 1.29 (d, 3 H, H-6).

Anal. Calc. for $C_{11}H_{20}O_6$: C, 53.21; H. 8.12. Found. C, 53.11; H, 7.89.

*Methyl 6-deoxy-2,4-di-O-methyl-α-*L*-*arabino*-hexopyranosid-3-ulose* (**9**) — Oxidation of **6** (1.0 g, 4.9 mmol) was achieved with ruthenium tetraoxide (0.1 g, 0.75 mmol), potassium carbonate (0.15 g, 1 mmol), and aqueous sodium periodate solution (1.24 g, 5.8 mmol) in carbon tetrachloride (30 mL) at room temperature. The mixture was stirred for 24 h, and monitoring by t.l.c. (5:1 benzene–ethyl acetate) showed the conversion of **6** into the product. The solid was filtered off, the filtrate was poured into water, and extracted with chloroform. On evaporation of the extract, the resulting syrup was purified on a column of silica gel; yield 0.73 g, 74%; m.p. 51–42°, $[\alpha]_D^{17}$ −167.4° (*c* 1, carbon tetrachloride); ν_{max}^{film} 1745 cm^{-1} (C=O); n.m.r.: δ 4.87 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 3.61 (d, 1 H, H-2), ~3.88 (m, 2 H, H-4,5), 3.38, 3.42, and 3.52 (each s, 9 H, 3 OMe), and 1.41 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6).

Anal. Calc. for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 52.70; H, 7.92%.

*Methyl 3,6-dideoxy-2,4-di-O-methyl-3-C-methylene-α-*L*-*arabino*-hexopyranoside* (**10**). — A 10% solution of butyllithium in hexane (20 mL, 31 mmol) was added dropwise, with stirring, to a suspension of methyltriphenylphosphonium bromide (11 g, 31 mmol) in dry oxolane (50 mL) cooled in an ice–water bath. To the resulting, yellowish suspension was then rapidly added a solution of **9** (4.0 g, 19.6 mmol) in oxolane (30 mL), with vigorous stirring, and the mixture was kept for 30 min at room temperature (until **9** disappeared; t.l.c.). Ether (200 mL) was added, the precipitate was removed by filtration, the filtrate was evaporated, the residue was extracted with dichloromethane, and the extract was washed with water, and evaporated; the residual syrup was purified on a column of silica gel with 100:1 benzene–acetone, to give syrupy **10** (2.6 g, 66% yield); $[\alpha]_D^{26}$ −171° (*c* 1.14, methanol); n.m.r.: δ 5.12 and 5.31 (each bt, 2 H, $J_{gem} = J_{4,CH_2} = 2.0$ Hz, *exo*-CH_2), 4.64 (d,

1 H. $J_{1,2}$ 1.5 Hz, H-1), 3.71 (d, 1 H, H-2), 3.52 (bd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.52 (oct, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 3.32, 3.36, and 3.47 (each s, 9 H, 3 OMe), and 1.32 (d, 3 H, H-6).

Anal. Calc. for $C_{10}H_{18}O_4$: C, 59.40; H, 8.19. Found: C, 59.63; H, 8.80.

Methyl 3,3^1-anhydro-6-deoxy-3-C-(hydroxymethyl)-2,4-di-O-methyl-α-L-mannopyranoside (**11**) *and methyl 3,3^1-anhydro-6-deoxy-3-C-(hydroxymethyl)-2,4-di-O-methyl-α-L-altropyranoside* (**12**). — A solution of **10** (2.5 g, 12.3 mmol) and *m*-chloroperoxybenzoic acid (80% purity; 2.34 g, 13.5 mmol) in 1,2-dichloroethane (100 mL) was stirred overnight at room temperature. The precipitate was removed by filtration, and the filtrate was successively washed with 0.1M sodium hydroxide and water, dried (magnesium sulfate), and evaporated to a syrup, which was purified on a column of silica gel with 1:1:1 hexane–chloroform–ether, to give a mixture of two epimers (each R_F 0.6) (1.5 g, 65% yield). The ratio of **11** to **12** was estimated to be 1:1 from the n.m.r. spectrum, but only **11** was isolated in pure state by preparative t.l.c. (5:1 benzene–acetone). Compound **11** had $[\alpha]_D^{27}$ −99.4° (*c* 1.09, methanol); n.m.r.: δ 4.63 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.7 (d, 1 H, H-2), 3.30 (d, 1 H, $J_{4,5}$ 8.5 Hz, H-4), 4.0 (oct, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 3.42 (s, 3 H, OMe), 3.44 (s, 6 H, 2OMe), 2.92 and 2.76 (ABq, *J* 5.0 Hz, CH_2-epoxy), and 1.34 (d, 3 H, H-6).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.04; H, 8.25. Found: C, 54 95; H, 8.25.

Methyl 6-deoxy-3-C-methyl-2,4-di-O-methyl-α-L-mannopyranoside (**13**). — Lithium aluminum hydride (0.18 g, 4.7 mmol) was gradually added to a solution of **11** (1 g, 4.58 mmol) in dry ether (5 mL). The mixture was boiled for 3 h under reflux, and cooled. Ethyl acetate and water were successively added to the mixture, and the precipitate was removed by filtration and washed with ether. The usual processing of the filtrate and washings, and purification of the products on a column of silica with 1:1:1 hexane–chloroform–ether, gave syrupy **13** (0.65 g, 65% yield), $[\alpha]_D^{17}$ −62° (*c* 1. methanol); n.m r.: δ 4.63 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.01 (d, 1 H, H-2), 2.88 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.4 (m, 1 H, H-5), 3.37, 3.43, and 3.55 (each s, 9 H, 3 OMe), 1.27 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6), and 1.29 (s, 3 H, CMe).

Anal Calc. for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 54.73; H, 9.02

Methyl 6-deoxy-3-C-methyl-2,4-di-O-methyl-α-L-altropyranoside (**14**). — To a suspension of magnesium turnings (1 g, 41 mmol) in dry ether (50 mL) was added methyl iodide (14 g, 98 mmol) dropwise, with stirring, at room temperature, and then **9** (2.7g, 13 mmol) in benzene (30 mL) was added to the Grignard solution. After being stirred for 1 h, the mixture was processed in the usual way, to give a syrup that was purified on a column of silica gel with 5:1 benzene–acetone, to give **14** (2.12 g, 72.8%) as the more polar portion, and **13** (0.53 g, 18%) as the less polar portion Compound **14** had $[\alpha]_D^{17}$ −63.6° (*c* 1, carbon tetrachloride); n.m.r.: δ 4.71 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.07 (d, 1 H, H-2), 2.89 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.81 (oct, 1H, $J_{5,6}$ 6.3 Hz, H-5), 3.44, 3.47, and 3.54 (each s, 9 H, 3 OMe), 3.65 (s, 1 H, OH), 1.37 (d, 3 H, H-6), and 1.35 (s, 3 H, CMe).

Anal. Calc. for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 54.18; H, 9.13.

Methyl 6-deoxy-3-C-methyl-2,3,4-tri-O-methyl-α-L-mannopyranoside (**15**). —

To a solution of **13** (0.45 g, 2 mmol) and sodium hydride (0.11 g, 4.5 mmol) in dimethyl sulfoxide (5 mL) was added methyl iodide (4.5 g, 31 mmol) at 0°. The solution was kept for 12 h at room temperature, with stirring, poured into cold water, and the resulting solution extracted with chloroform. The extract was evaporated, to give syrupy **15** (0.4 g, 85% yield), which was sublimed at 40°/0.03 mm Hg. Some physical properties of **15** are shown in Table I.

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.39; H, 9.47. Found: C, 56.45, H, 9.31.

6-Deoxy-3-C-methyl-2,3,4-tri-O-methyl-L-mannose (**1**, L-*Nogalose*). — A solution of **15** (0.1 g, 0.43 mmol) in 0.5M sulfuric acid (4 mL) was maintained for 30 min at 90°, cooled, the acid neutralized with barium carbonate, and the suspension filtered. The filtrate was evaporated, and the residue, which crystallized from ethyl acetate, was sublimed at 60°/0.01 mm Hg, to give **1** (74 mg, 78% yield), m.p. 110–115°, $[\alpha]_D^{17}$ −14 → −8.4° (*c* 1, methanol; 24 h) {lit.[2] m.p. 115–121°, $[\alpha]_D^{25}$ −10.6° (*c* 1, methanol), $[\alpha]_D$ −17.1 → −5.1° (24 h; methanol)}; m.s., molecular-ion peak: found 220 (calc. 220).

Anal. Calc. for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 54.45, H, 8.94.

Methyl 4-O-benzoyl-6-bromo-6-deoxy-3-C-methyl-α-D-mannopyranoside (**17**). — A mixture of **16** (0.21 g, 0.67 mmol), barium carbonate (0.33 g, 1.67 mmol), and *N*-bromosuccinimide (0.2 g, 1.12 mmol) in dry carbon tetrachloride (20 mL) was boiled for 4 h under reflux, cooled, filtered, and the filtrate successively washed with aqueous sodium hydrogencarbonate and water, and evaporated, to give **17** as white crystals; m.p. 86–88°, $[\alpha]_D^{28}$ +23° (*c* 0.8, methanol); n.m.r.: δ 8.12–8.0 and 7.6–7.3 (m, 5 H, PhCO), 4.88 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.18 (d, 1 H, H-2), 5.17 (d, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.98 (dq, 1 H, $J_{5,6}$ 11.5, $J_{5,6'}$ 6.5 Hz, H-5), 3.4–3.6 (m, 2 H, H-6,6'), 3.50 and 3.53 (each s, 6 H, 2 OMe), 3.0 (s, 1 H, OH), and 1.46 (s, 3 H, CMe).

Anal. Calc. for $C_{16}H_{21}BrO_6$: C, 49.35; H, 5.39. Found: C, 49.75; H, 5.36.

Methyl 4-O-benzoyl-6-deoxy-3-C-methyl-2-O-methyl-α-D-mannopyranoside (**18**). — A solution of **17** (70 mg, 0.18 mmol) and tributylstannane (200 mg, 0.69 mmol) in dry benzene (5 mL) was boiled under reflux in the presence of α,α'-azobis(isobutanonitrile) for 2 h, the reaction being monitored by t.l.c. (hexane–ether), which then indicated complete conversion into product. The solution was now evaporated, and the residue was placed on column of silica gel. The stannane compound was removed by using hexane as the eluant, and, thereafter, elution with 1:1 hexane–ether gave syrupy **18** (46 mg, 81% yield), $[\alpha]_D^{28}$ +23.7° (*c* 1.1, methanol); n.m.r.: δ 8.15–8.0 and 7.7–7.3 (m, 5 H, PhCO), 4.81 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.16 (d, 1 H, H-2), 5.10 (d, 1 H, $J_{4,5}$ 10 Hz, H-4), 3.90 (oct, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 3.42 and 3.51 (each s, 6 H, 2 OMe), 1.24 (d, 3 H, H-6), and 1.44 (s, 3 H, CMe).

Anal. Calc. for $C_{16}H_{22}O_6$: C, 61.93; H, 7.09. Found: C, 61.95; H, 7.21.

Methyl 6-deoxy-3-C-methyl-2-O-methyl-α-D-mannopyranoside (**19**). — A solution of **18** (0.3 g, 0.96 mmol) in methanol presaturated with ammonia (70 mL) was kept for 15 h at room temperature, and then evaporated to a syrup. The syrup was extracted with petroleum ether, and the extract was evaporated, to give a syrup which was purified on a column of silica gel with 4:1 benzene–acetone, to give syrupy **19**;

yield, quantitative: $[\alpha]_D^{28}$ +41° (*c* 0.5, methanol); n.m.r.: δ 4.74 (d, 1 H, $J_{1,2}$ 2.0 Hz, H-1), 3.13 (d, 1 H, H-2), 3.07 (d, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.54 (oct, 1 H, $J_{5,6}$ 6.0 Hz, H-5), 3.38 and 3.48 (each s, 6 H, 2 OMe), 1.88 and 2.36 (each s, 2 H, 2 OH), 1.30 (d, 3 H, H-6), and 1.32 (s, 3 H, CMe).

Anal. Calc. for $C_9H_{18}O_5$: C, 52.42; H, 8.73. Found: C, 52.41; H, 8.74.

*Methyl 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-α-*D*-mannopyranoside* (**20**). — Methylation of **19**, as for **5**, gave the corresponding methylation product (**20**) in 88% yield. Some physical constants of **20** are given in Table I.

Anal. Calc. for $C_{11}H_{22}O_5$: C, 56.39; H, 9.47. Found: C, 56.41; H, 9.46.

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