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SYNTHESIS OF METHYL 2,3-DI-*o*-METHYL-α-D-SIBIROSAMINIDE

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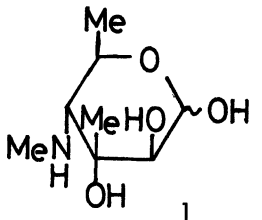
Methyl 2,3-di-*o*-methyl-α-D-sibirosaminide (12; methyl 4,6-dideoxy-3-*c*-methyl-2,3-di-*o*-methyl-4-methylamino-α-D-altropyranoside) has been synthesized from methyl 4,6-*o*-benzylidene-3-*c*-methyl-2-*o*-methyl-α-D-altropyranoside (2). The introduction of methylamino group at *c*-4 position was achieved by hydrogenation of methyl 6-deoxy-3-*c*-methyl-2,3-di-*o*-methyl-α-D-*arabino*-hexopyranosid-4-ulose oxime (8) in the ratio of 2.6:1 (altro:ido) followed by *N*-formylation and reduction.

Sibrosamine, a component sugar of sibiromycin, an antitumor antibiotic produced by *streptosporangium sibiricum*[1] was characterized as 4,6-dideoxy-3-*c*-methyl-4-methylamino-D-altropyranose (1).[2] Recently, Dyong[3] and his co-workers have reported the synthesis of methyl 2-*o*-acetyl-4,6-dideoxy-3-*c*-methyl-4-tosylamino-α-D-altropyranoside, as a key intermediate for the synthesis of sibirosamine, through [2,3]-sigmatropic rearrangement of the corresponding 3-*c*-methyl-hex-2-enopyranoside followed by vicinal *cis*-oxyamination of the C=C bond.[4]

In this communication, the synthesis of methyl 4,6-dideoxy-3-*c*-methyl-2,3-di-*o*-methyl-4-methylamino-α-D-altropyranoside (12) from methyl 4,6-*o*-benzylidene-3-*c*-methyl-2-*o*-methyl-α-D-altropyranoside (2),[5] through successive deoxygenation of *c*-6 and methylamination of *c*-4 positions, is described.



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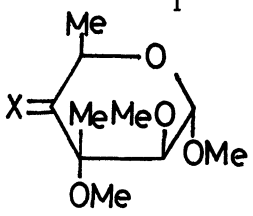
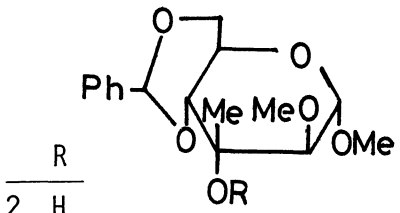
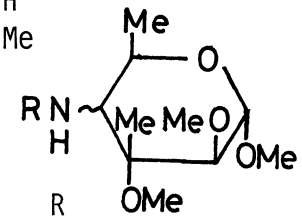


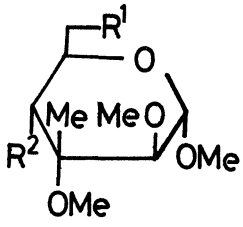
X	
7	O
8	NOH



R	
2	H
3	Me



R	
9	H
10	Ac
11	CHO



R^1	R^2	
4	Br	OBz
5	H	OBz
6	H	OH
12	H	NHMe

Compound (2) was 3-*O*-methylated by the usual procedure, and the product (3) 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-altropyranoside (4), mp 136-138°C: $[\alpha]_D^{18}$ +56° (*c* 1.0, MeOH); NMR: δ4.79(d, $J_{1,2}$=2 Hz, H-1), 3.52(d, H-2), 5.24(d, $J_{4,5}$=9.5 Hz, H-4), 4.50(oct, $J_{5,6}$=$J_{5,6'}$=6 Hz, H-5), 3.4-3.6(m, H-6 and H-6'), 8.19-8.0 and 7.7-7.3(m, Ph), 3.32, 3.47(3×OMe), 1.26(s, CMe), in 75% yield. Reduction of (4) in benzene with tributylstannane in the presence of α,α'-azo-bis-isobutyronitrile gave the corresponding 6-deoxy derivative (5), mp 103-104°C; $[\alpha]_D^{18}$ +58° (*c* 1.0, MeOH); NMR: δ4.72(s, H-1), 3.36(s, H-2), 5.17(d, $J_{4,5}$=9.5 Hz, H-4), 4.30(oct, H-5), 1.21 (d, $J_{5,6}$=7 Hz, H-6), 8.20-8.05 and 7.7-7.38(m, Ph), 3.37, 3.45 and 3.49(3×OMe), 1.28(s, CMe), in 70% yield. Treatment of (5) with sodium methoxide gave the required de-*O*-benzoylated product (6) as a syrup, $[\alpha]_D^{18}$ +38° (*c* 1.0, MeOH); NMR: δ4.60(s, H-1), 3.48(s, H-2), 3.16(d, $J_{4,5}$=10 Hz, H-4), 3.82(oct, H-5), 1.30(d, $J_{5,6}$ =6 Hz, H-6), 2.16(d, J=12 Hz, OH), 3.25, 3.37 and 3.41(3×OMe), 1.32(s, CMe), in 90% yield. The oxidation of (6) with dimethyl sulfoxide-trifluoroacetic anhydride in methylene dichloride gave the corresponding 4-ulose (7) as a syrup, $[\alpha]_D^{18}$ +190° (*c* 1.7, MeOH); IR: $\nu_{C=O}$ 1740 cm^{-1}; NMR: δ4.68(d, $J_{1,2}$=4 Hz, H-1), 3.61(d, H-2), 4.18 (q, $J_{5,6}$=7.5 Hz, H-5), 1.34(d, H-6), 3.33, 3.43 and 3.52(3×OMe), 1.44(s, CMe), in 80% yield.

The oximation of (7) with hydroxylamine hydrochloride and sodium acetate in aq. methanol gave methyl 6-deoxy-3-*C*-methyl-2,3-di-*O*-methyl-α-D-*arabino*-hexopyranosid-4-ulose oxime (8), mp 65-67°C; $[\alpha]_D^{14}$ +124° (*c* 1.5, MeOH); NMR: δ4.57(d, $J_{1,2}$=2 Hz, H-1), 3.35(d, H-2), 4.87(q, $J_{5,6}$=7.5 Hz, H-5), 1.49(d, H-6), 3.38, 3.38 and 3.46 (3×OMe), 8.7(s, NOH), 1.51(s, CMe), in 91% yield. Hydrogenation of (8) in glacial acetic acid in the presence of platinum oxide gave a mixture of *altro* and *ido* derivatives (9), IR: ν_{NH_2} 3250 and 3450 cm^{-1}, in 60% yield. The ratio of the two isomers was determined from the NMR spectrum of acetylated products (10) to be 2.6:1 [altro (δ3.94, $J_{4,5}$=5.8 Hz, H-5): ido (δ4.38, $J_{4,5}$=2.0 Hz, H-5)]. The *N*-formylation of (9) with p-nitrophenyl formate in tetrahydrofuran gave *N*-formyl derivative (11) in 76% yield, which was reduced with lithium aluminium hydride in benzene-ether to give a mixture of *N*-methyl derivatives in 85% yield. Separation of the mixture on a silica gel column using chloroform as eluent gave pure (12) of D-altro configuration as a syrup, $[\alpha]_D^{15}$ +67° (*c* 0.9, MeOH), NMR: δ4.59(s, H-1), 3.35(s, H-2), 2.35(d, $J_{4,5}$=10 Hz, H-4), 3.80(oct, $J_{4,5}$=10, $J_{5,6}$=6 Hz, H-5), 1.26(d, H-6), 3.42, 3.36 and 3.22(3×OMe), 2.50(s, NMe), 1.30(s, CMe).

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References

1) G. F. Cause, T. P. Preobrazhenskaia, L. P. Invanitskaya, and M. A. Sveskarikova, Antibiotiki, 14, 963 (1969).
2) A. S. Mesentsev, V. V. Kuliaeva and L. M. Rubasheva, J. Antibiotics, 1974, 866.
3) I. Dyong and G. Schulte, Tetrahedron Lett., 21, 603 (1980).
4) K. B. Sharpless, A. O. Chong and K. Oshima, J. Org. Chem., 41, 177 (1976).
5) K. Sato and J. Yoshimura, Bull. Chem. Soc. Jpn., 51, 2116 (1978).

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