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THE SYNTHESIS OF D-EVALOSE

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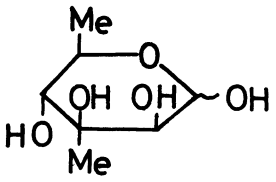
D-Evalose (1: 6-deoxy-3-*C*-methyl-D-mannose) was synthesized from methyl 3,3'-anhydro-4,6-*O*-benzylidene-3-*C*-hydroxymethyl-2-*O*-methyl-α-D-mannopyranoside (3) through five-step derivations, and the structure was confirmed by the conversion into D-nogaloside (8: methyl 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-α-D-mannopyranoside).

D-Evalose (1) was found as a component sugar of everninomicin B and its absolute configuration was established by Ganguly and Saksena[1] by conversion into D-nogalose, the enantiomer of the component sugar of nogalamycin.[2]

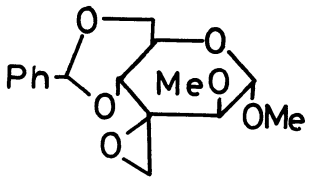
Recently, we have synthesized L-nogalose, in which the *C*-methyl branching was introduced by successive epoxidation and reduction of methyl 3,6-dideoxy-2,4-di-*O*-methyl-3-*C*-methylene-α-L-*arabino*-hexopyranoside obtained from L-rhamnose.[3] In addition, it was also reported that the peroxy acid oxidation of methyl 4,6-*O*-benzylidene-2-*O*-methyl-3-*C*-methylene-α-D-*arabino*-hexopyranoside (2), which was derived *via* the corresponding 3-ulose obtained by dimethyl sulfoxide-trifluoroacetic anhydride oxidation of methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-altropyranoside,[4] gave preferentially the corresponding spiro-epoxide (3) of D-*manno* configuration.[5]

This communication describes the first facile synthesis of D-evalose by reduction of the epoxy ring of (3) and subsequent deoxygenation at C-6 position.

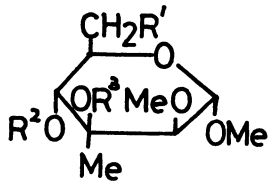
Reduction of (3) with lithium aluminium hydride in tetrahydrofuran gave methyl 4,6-*O*-benzylidene-3-*C*-methyl-2-*O*-methyl-α-D-mannopyranoside [4: sirup] in 73% yield. Treatment of (4) with *N*-bromosuccinimide in carbon tetrachloride gave methyl 4-*O*-benzoyl-6-bromo-6-deoxy-3-*C*-methyl-2-*O*-methyl-α-D-mannopyranoside [5: mp 86-88°C, $[\alpha]_D^{28}$ +23° (*c* 0.8, MeOH), NMR: δ4.88 (d, $J_{1,2}$=2.0 Hz, H-1), 3.18 (d, H-2), 5.17 (d, $J_{4,5}$=10 Hz, H-4), 3.98 (oct, $J_{5,6}$=11.5, $J_{5,6'}$=6.5 Hz, H-5), 3.4-3.6 (m, H-6 and H-



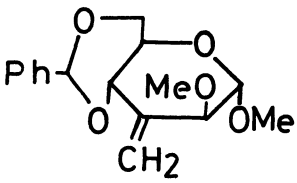
(1)



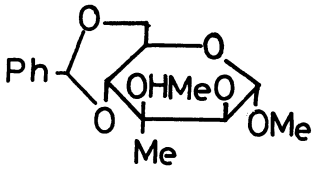
(3)



(5) R^1 = Br R^2 = Bz R^3 = H
(6) R^1 = H R^2 = Bz R^3 = H
(7) R^1 = H R^2 = H R^3 = H
(8) R^1 = H R^2 = Me R^3 = Me



(2)



(4)

6'), 8.12-8.0 and 7.6-7.3 (m, Ph), 3.50 and 3.53 (2 × OMe), 3.0 (broad s, OH), 1.46 (s, C-Me)] in 65% yield. Reduction of (5) in benzene with tributylstannane in the presence of α,α'-azobis-isobutyronitrile gave corresponding 6-deoxy derivative [6: sirup, $[\alpha]_D^{28}$ +23.7° (*c* 1.1, MeOH), NMR: δ4.81 (d, $J_{1,2}$=2.0 Hz, H-1), 3.16 (d, H-2), 5.10 (d, $J_{4,5}$=10 Hz, H-4), 3.90 (dq, H-5), 1.24 (d, $J_{5,6}$=6.5 Hz, H-6), 8.15-8.0 and 7.7-7.3 (m, Ph), 3.42 and 3.51 (2 × OMe), 1.44 (C-Me)] in 81% yield. Treatment of (6) with methanolic ammonia gave the corresponding de-*O*-benzoylated product [7: sirup, $[\alpha]_D^{28}$ +41° (*c* 0.5, MeOH)] in quantitative yield. De-*O*-methylation of (7) in methylene chloride with boron trichloride[6] at -78°C for 30 min. gave D-evalose as a colorless glass [1: $[\alpha]_D^{28}$ -4.7° → -5.2° (water, 24 h), lit.,[1] $[\alpha]_D$ -4.7° → -5.2° (water)], in a good yield.

For the further characterization, (7) was O-methylated with sodium hydride and methyl iodide in *N*,*N*-dimethylformamide gave methyl D-nogaloside [8: mp 42°C, $[\alpha]_D^{30}$ +50° (*c* 0.64, MeOH), NMR: δ4.72 (d, $J_{1,2}$=2.0 Hz, H-1), 3.37 (d, H-2), 3.07 (d, $J_{4,5}$=9.5 Hz, H-4), 3.60 (m, H-5), 1.28 (d, $J_{5,6}$=6.2 Hz, H-6), 1.31 (C-Me), 3.27, 3.36, 3.48 and 3.53 (each s, 4 × OMe)] in 88% Yield. Physical constants of (8) were completely identical with those of L-nogaloside[2,3] except the reverse sign of rotational value.

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