The Synthesis of D-Arcanose

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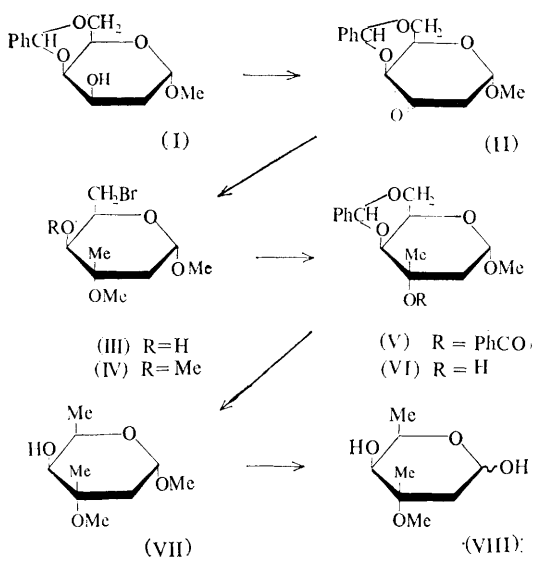
ARCANOSE, a carbohydrate which occurs as the 4-*O*-acetyl derivative in the medium-spectrum macrolide antibiotic lankamycin, has been shown to be 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-L-*xylo*-hexose [see (VIII) for the D-enantiomer] on the basis of chemical degradation and n.m.r. data.[1] Here we report the synthesis of the D-enantiomer, which corroborates the structure and stereochemistry previously assigned to arcanose.

Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*lyxo*-hexopyranoside (I) was obtained by standard procedures from D-galactal,[2] and on oxidation with a mixture of ruthenium dioxide and potassium metaperiodate in chloroform, in the presence of potassium carbonate,[3] gave methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*threo*-hexopyranosid-3-ulose (II)[4] in 89% yield. A solution of (II) in benzene was treated with methylmagnesium iodide in ether at 0° to give predominantly methyl 4,6-*O*-benzylidene-2-deoxy-3-*C*-methyl-α-D-*xylo*-hexopyranoside (III)† as a syrup (91%) which had $[\alpha]_D$ + 159° (*c*, 1·1). Treatment of (III)

† All new compounds gave satisfactory elemental analyses, and gave infrared and n.m.r. spectra in agreement with the assigned structures. Optical rotations were measured at 20 ± 2° in chloroform, unless otherwise stated. N.m.r. data refer to deuteriochloroform solutions, with tetramethylsilane as internal standard.

with dimethyl sulphate and sodium hydroxide in tetrahydrofuran gave the 3-*O*-methyl derivative (IV) in 82% yield, m.p. 38—39°, $[\alpha]_D$ + 119° (*c*, 0·8). Compound (IV) was converted into methyl 4-*O*-benzoyl-6-bromo-2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-α-D-*xylo*-hexopyranoside (V) by treatment with *N*-bromosuccinimide according to the procedure described recently by Hanessian[5] for ring-opening of benzylidene acetals of sugars. The product was a syrup (91%) and had $[\alpha]_D$ + 134° (*c*, 0·9). Treatment of a methanolic solution



of (V) with a catalytic amount of sodium methoxide gave methyl 6-bromo-2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-α-D-*xylo*-hexopyranoside (VI), which crystallized (86%) from pentane and had m.p. 62—63°, $[\alpha]_D$ + 134° (*c*, 0·7). Reduction of the 6-bromo-derivative (VI) with lithium aluminium hydride gave methyl 2,6-dideoxy-3-*C*-methyl-3-*O*-methyl-α-D-*xylo*-hexopyranoside (VII) in 62% yield, m.p. 93—94°, $[\alpha]_D$ + 167° (*c*, 0·7). Acid-catalyzed hydrolysis with Rexyn 101 (H) ion-exchange resin of the glycoside (VII) finally afforded D-arcanose (VIII), which had m.p. 101—102° and $[\alpha]_D$ + 19·8° (*c*, 1 ethanol). Keller-Schierlein and Roncari[6] have reported m.p. 96—98° and $[\alpha]_D$ −19·2° (*c*, 4·6 ethanol) for the L-enantiomer. The infrared and n.m.r. spectra of the synthetic product were identical with those of authentic L-arcanose,‡ and the two compounds were indistinguishable by paper and thin-layer chromatography.

Acetylation of (III) with acetyl chloride–dimethylaniline[7] gave a syrupy acetate whose n.m.r. spectrum showed an acetyl signal at τ 8·04. Tertiary acetoxy-groups possessing the axial orientation in a number of cyclanols have been reported[8] recently to give n.m.r. signals in the region τ 7·93—8·04. With (III) in the *C*1 (D) conformation, this n.m.r. data supports the previously assigned *xylo*-configuration for arcanose.[1]

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