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# IDENTIFICATION OF THE 2-HYDROXYMETHYL-3,4-DIHYDROXYPYRROLIDINE (OR 1,4-DIDEOXY-1,4-IMINOPENTITOL) FROM ANGYLOCALYX BOUTIQUEANUS AND FROM ARACHNIODES STANDISHII AS THE (2R, 3R, 4S)-ISOMER BY THE SYNTHESIS OF ITS ENANTIOMER.

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Summary. The D-xylo and L-arabino isomers of 1,4-dideoxy-1,4-iminopentitol have been synthesised from L-arabinose, and the L-arabino isomer was found to be the enantiomer of the alkaloid from Angylocalyx Boutiqueanus. The alkaloid from Arachniodes Standishii, recently reported to have the xylo configuration, was also shown to be the D-arabino isomer.

Naturally occurring hydroxylated piperidine derivatives such as 1,5-dideoxy-1,5-imino-D-mannitol[1] and 1,5-dideoxy-1,5-imino-D-glucitol (deoxynojirimycin)[2] are of considerable current interest because of their inhibitory action on glycosidases[2,3]. A 1,4-dideoxy-1,4-iminopentitol (1) recently isolated from Arachniodes Standishii was assigned the xylo configuration on the basis of proton-proton coupling constants. We have recently reported the identification of two new pyrrolidine derivatives namely 2-hydroxymethyl-3,4-dihydroxyrrolidine (1) of unknown configuration[5] and (2R, 3S)-2-hydroxymethyl-3-hydroxypyrrolidine[6]. The former pyrrolidine derivative has now been identified as 1,4-dideoxy-1,4-imino-D-arabinitol by synthesis of its enantiomer.

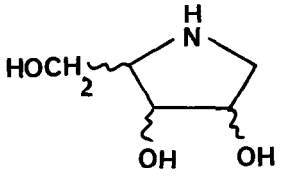
The D-xylo isomer of (1) was first synthesised from 4-azido-4-deoxy-D-xylose[7] which is readily prepared in six steps from L-arabinose. Catalytic hydrogenation of the azide over palladium in methanol containing acetic acid first formed the primary amine and reductive amination[8] then followed to give 1,4-dideoxy-1,4-imino-D-xylitol[9] as the acetate salt in 88% yield [$\delta_c$($D_2O$) 77.1(X2), 65.7, 60.0, 53.3 with dioxane reference at 69.3 p.p.m]. The hydrochloride had $[\alpha]_D^{20}$ + 12° ($H_2O$) and gave the same chemical shifts which are different from those reported[4] for the alkaloid from Arachniodes Standishii.

The L-arabino isomer of (1) was also synthesised from L-arabinose by means of a double inversion at C-4. This was accomplised in two ways. Methyl 2,3-di-O-benzoyl-β-L-arabinopyranoside[7] was quantitatively converted into the triflate (m.p. 119-121°) which on reaction with sodium nitrite in DMF at room temperature[10] gave methyl 2,3-di-O-benzoyl-α-D-xylopyranoside (m.p. 129-131°, 81%). The D-xylo configuration was confirmed by the proton n.m.r. spectrum; the two pyranose protons deshielded by the benzoyloxy groups were double doublets at δ 5.69 (H-3, $J_{3,4}$ 8.5, $J_{2,3}$ 10.0 Hz) and 5.20 (H-2, $J_{1,2}$ 3.7 Hz); H-4 gave a multiplet at δ4.0. The derived 4-O-tosylate (m.p. 180-183; 81%) was reacted with sodium azide in DMF at 100°C to give methyl 4-azido-2,3-di-O-benzoyl-4-deoxy-β-L-arabinopyranoside (m.p. 104-105.5°, 85%, $J_{3,4}$ 4 Hz).

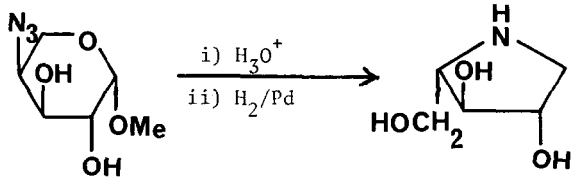
Alternatively the double inversion and introduction of the azide function at C-4 could be effected in two steps by reacting methyl β-L-arabinoside 2,3-dibenzoate with triphenylphosphine and 2,4,5-tribromoimidazole[11] to form the methyl 2,3-di-O-benzoyl-4-bromo-4-deoxy-D-xylopyranoside[12] in 81% yield (after chromatography, m.p. 112-114.5°). This bromide reacted cleanly with sodium azide in DMF at 86° over three days to form the L-arabinoside azide in 81% yield. This two step conversion of methyl 2,3-di-O-benzoyl-β-L-arabinopyranoside into

the 4-azido-4-deoxy-L-arabinoside via the bromide (overall yield 66%) was more efficient than the four steps above via the triflate (overall yield 56%). The bromide required column chromatography for isolation whereas the triflate involved the use of the relatively expensive triflic anhydride.

Debenzoylation of the azide dibenzoate with methanolic sodium methoxide gave methyl 4-azido-4-deoxy-β-L-arabinopyranoside (2), (m.p. 86-88°). Acid hydrolysis and catalytic hydrogenation[8] over palladium in aqueous acetic acid gave 1,4-dideoxy-1,4-imino-L-arabinitol as a syrup which, after treatment with Amberlite CG 400 ($OH^-$ form), was identical by $^1H$ and $^{13}C$ n.m.r. spectroscopy to the natural product[5]. The hydrochloride had $[\alpha]_{578}^{20}$ - 22° ($H_2O$) and was the enantiomer of the Angylocalyx Boutiqueanus alkaloid which has $[\alpha]_{578}^{20}$ + 25° (± 3°) (c, 0.3 in $H_2O$). The $^{13}C$ chemical shifts of the hydrochloride were identical to those reported for the Arachniodes Standishii alkaloid[4] which must therefore have the arabino configuration. The specific rotation (+ 4.7° at 550 and 589 Å) of this alkaloid implies the D-enantiomer, although the values are not in good agreement[13].




(1)




(2) (3)

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