OLIVOMYCIN AND RELATED ANTIBIOTICS

XXVII.* A NEW NATURAL MONOSACCHARIDE – D-MYCAROSE

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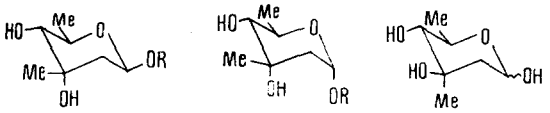
In the hydrolysis of the antibiotics, olivomycins A, B, C, and D, we isolated the monosaccharides olivomycose, oliose, olivomose, and olivose and acyl derivatives of the first two of them [2]. The same monosaccharides have been found in antibiotics related to the olivomycins – the chromomycins A_2, A_3, and A_4 [3]. In an investigation of the parent antibiotic of this group – aureolic acid [4, 5] – we have found that it contains yet another carbohydrate component, a (+)-monosaccharide $C_7H_{14}O_4$.

The NMR spectrum of this monosaccharide (Fig. 1) shows that it is a 3-C-methyl-2,6-dideoxyaldohexose. In actual fact, the substance contains secondary and tertiary C-methyl groups (doublet at 1.27 ppm, J = 6 Hz, and singlet at 1.28 ppm, respectively). The signal of the anomeric proton forms a quartet with J = 10 and 3 Hz, from which it follows that this proton is oriented axially† and there is a methylene group in position 2. The protons of this group together with H_1 form an isolated ABX system with δ_{2a} 1.62, δ_{2e} 2.03, and δ_1 5.17 ppm, $J_{2a:2e} = 14$, $J_{2a:1} = 10$, and $J_{2e:1} = 3$ Hz. Since H_{2a} and H_{2e} do not participate in other interactions, there are no protons on the neighboring carbon atom (C_3), and this atom is the cite of branching of the chain. This conclusion is confirmed by the results of periodate oxidation, in which 2 moles of IO_4^- were consumed, and 1 mole of HCOOH, but no malondialdehyde, was formed. The H_4 proton is represented in the NMR spectrum by a doublet at 3.10 ppm with J = 10 Hz; the large value of J shows that there is no free rotation round the C_4-C_5 bond (i.e., the sugar is in the pyranose form) and the H_4 and H_5 protons are in the trans-diaxial positions.

Of the two anomeric methyl glycosides of this sugar, the levorotatory must be the β isomer, since in it the H_1 proton is oriented axially (the signal of this proton in the NMR spectrum consists of a quartet at 4.61 ppm with J = 9 and 3 Hz). According to the isorotation rule, the sugar under consideration has the D configuration.



I R=H
II. R=Me

Ia. R=H
III. R=Me

IV

On the basis of the facts presented, only two structures are possible for the sugar: D-mycarose (I ⇌ Ia) and D-olivomycose (IV), the L enantiomers of which are present in a number antibiotics [3, 6-11]. The results of a direct comparison of the monosaccharide under investigation with samples of L-mycarose from carbomycin [6] and of L-olivomycose from the olivomycins [11] showed that it was D-mycarose (I ⇌ Ia) and, consequently, its methyl α- and β-glycosides correspond to structures (III) and (II), respectively.

*For Communication XXVI, see [1].

†More accurately, the substance is a mixture of anomers in which the β isomer (I) with an equatorial glycosidic hydroxyl considerably predominates. The presence of a small amount of the α anomer (Ia) is shown in the spectrum by additional peaks of low intensity, for example, in the region of the H_4 signal.

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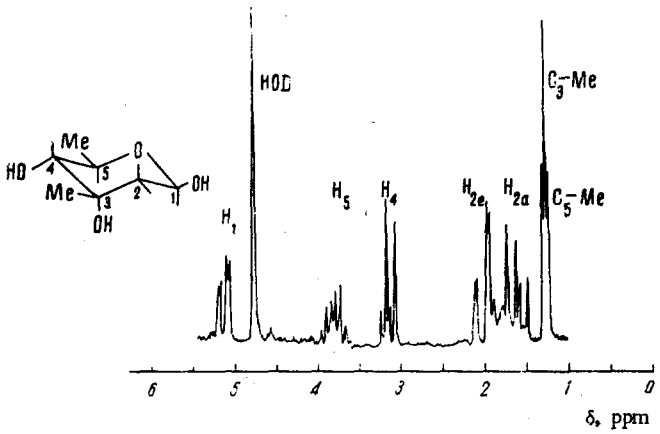

Fig. 1. NMR spectrum of D-mycarose (100 MHz, D_2O, internal standard sodium dimethylsilapentanesulfonate).

Aureolic acid is the first natural glycoside in which this sugar has been found; it has previously been obtained only synthetically [12].

EXPERIMENTAL

The D-mycarose (3-C-methyl-2,6-dideoxy-D-ribohexose) (I⇌Ia) was isolated from a hydrolysate of aureolic acid as described in a previous paper [13] in the form of a mixture of the two anomers with R_f 0.38 and 0.63 [silica gel, benzene–acetone (1 : 1) system] and R_f 0.65 [Whatman No. 2 paper, butan-1-ol–ethanol–water (4 : 1 : 5) system]. The substance crystallizes from ethyl acetate in two forms, with mp 102-105°C (polyhedrons) and 129-130°C (needles), $[\alpha]_D^{24}$ + 8.5°(immediately after dissolution), + 32° (after 48 h, c 0.7 in water). The nature of the mutarotation is the same for both crystalline forms. The NMR spectrum is shown in Fig. 1.

When this sugar was subjected to periodate oxidation under standard conditions [11], the consumption of oxidizing agent (in moles/mole) was: after 5 min 1.2, after 10 min 1.5, after 20 min 1.8, after 30 min 1.9, after 45 min 2.0 (with no further change during 2 h); titration of the liberated formic acid with 0.01 N NaOH (to phenolphthalein) gave a value of 0.9 mole/mole.

Methyl α- and β-D-Mycarosides (VIII) and (IX). A solution of 100 mg of D-mycarose (VII) in 10 ml of 0.05 N methanolic HCl was boiled for 2.5 h, and after cooling it was neutralized with Ag_2CO_3, filtered, and evaporated. The residue was chromatographed on silica gel in the benzene–acetone (5 : 1) system. The zone with R_f 0.41-0.43 yielded 22 mg (20%) of methyl α-mycaroside (VIII), $[\alpha]_D^{22}$ + 128° (c 0.4; ethanol), δ 1.17 (3H, s; C_3-Me), 1.27 (3H, d, J = 6; (C_5-Me), 1.71 (1H, 2d, J = 4 and 14; H_{2a}); 2.02 (1H, 2d, J = 1 and 14; H_{2e}), 2.00 (1H, d, J = 9; H_4), 3.30 (3H, s, O_1-Me), 3.4-3.6 (1H, m; H_5), 4.68 (1H, poorly resolved signal with a half-width of 7 Hz; H_1).

The zone with R_f 0.23-0.26 yielded 52 mg (47%) of methyl β-mycaroside (IX), $[\alpha]_D^{22}$ −31° (c 0.6; ethanol) δ 1.17 (3H, s, C_3-Me), 1.27 (3H, d, J = 6; C_5-Me), 1.55 (1H, 2d, J = 14 and 9; H_{2a}), 2.02 (1H, 2d, J = 14 and 3; H_{2e}), 3.00 (1H, d, J = 9; H_4), 3.40 (3H, s, O_1-Me), 3.4-3.7 (1H, m; H5), 6.61 (1H, q, J = 9 and 3; H_4).

The sample of carbomycin was kindly given to us by D. P. Pyatykhina (N. F. Gamaleya Institute of Microbiology and Epidemiology, Moscow).

SUMMARY

The structure of a new natural monosaccharide isolated from aureolic acid has been established. It is D-mycarose (3-C-methyl-2,6-dideoxy-D-ribohexose) (I ⇌Ia).

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