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THE SYNTHESIS OF N-BENZOYLRISTOSAMINE

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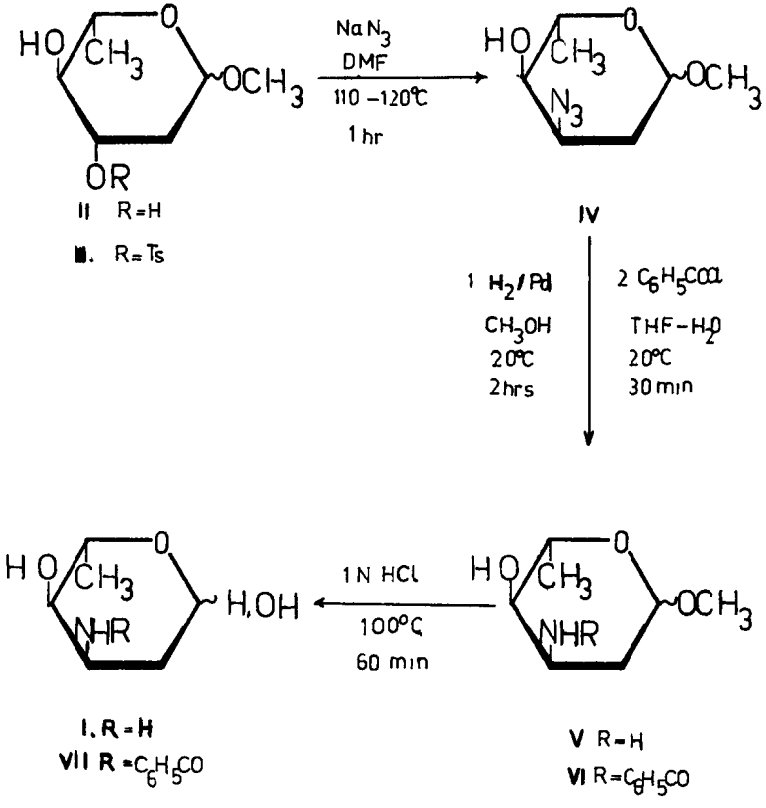
The antibiotic ristomycin isolated from Proactinomyces fructiferi var. ristomycini[1] is composed of an unusual peptide-aglycone moiety[2], a tetrasaccharide side chain[3] — containing neutral sugars — and a new amino sugar (ristosamine) to which the structure 2,3,6-trideoxy-3-amino-L-ribo-hexopyranose (I) has been assigned[4] on the basis of chemical and spectroscopic evidence.

The structure of ristosamine (I) is now substantiated by the following synthesis of 3-benzamido-2,3,6-trideoxy-L-ribo-hexopyranose (VII, N-benzoylristosamine).

Methoxymercuration[5] of L-rhamnal[6] followed by reduction with sodium borohydride[7] gave a mixture of methyl 2,6-dideoxy-α- and β-L-arabino-hexopyranoside (II) $\left[[\alpha]_D^{23}$ -118°(c 1.2, water); anal. calcd. for $C_7H_{14}O_4 \cdot OCH_3$, 19.13 %; found: OCH_3, 19.13 %; n.m.r. (100 MHz, $CDCl_3$): δ 1.28 (d, J = 6 Hz, CH_3); 1.45-2.30 (m, 2H, $>CH_2$); 3.33 (s, 3H, OCH_3)$\right]$; this was treated with p-toluenesulfonyl chloride in abs. pyridine at 0 °C for seven days. The resulting 3-O-monotoluene-p-sulfonate (III) was purified by column chromatography on Kieselgel G with 9·1 abs. benzene-methanol as the eluant $\left[[\alpha]_D^{23}$ -110° (c 1, chloroform), lit.[8] $[\alpha]_D$ -116° (chloroform); m.p. 79-81 °C, lit.[8] m.p. 86.5-86.9 °C; anal. calcd. for $C_{14}H_{20}O_6S$: S, 10.13 %; found: S, 10.31 %; n.m.r. (100 MHz, $CDCl_3$)· δ 1.14 (d, J=6 Hz, 3H, CH_3; the proportion of α and β anomers is ~4:1); 1.5-2.3 (m,


HO
CH3
O
OCH3
OR
NaN3
DMF
110 –120°C
1 hr
N3
II R=H
III. R=Ts
IV
1 H2/Pd
CH3OH
20°C
2hrs
2 C6H5COCl
THF–H2O
20°C
30 min
NHR
1N HCl
100°C
60 min
H,OH
I. R=H
VII R=C6H5CO
V R=H
VI R=C6H5CO

2H, $>CH_2$); 2.46 (s, 3H, tosyl CH_3); 3.28 (broad s, 3H, OCH_3); 7.2-7.8 (4H, aromatic)].

Displacement of the p-toluenesulfonyl group from III was achieved with azide ion in DMF at 110-120 °C. The crystalline azide (IV) [m.p. 96-97 °C; i.r. (film): ν_{C-N} 2100 cm^{-1}; t.l.c. R_f 0.46 (abs. benzene methanol = 9:1)] was obtained on purification by column chromatography under the same conditions as described for III. Although the molecular ion does not appear in the mass spectrum of IV, the fragments support its structure. Intensive loss of N_3 from the m/e 155 ion supports allylic (C-3) position of the azido group to the double bond of the $(M-CH_3OH)^+$ ion [m/e (I %): 155.0698(100), $M-CH_3OH$; 129(6); 113.0605(30), $M-CH_3OH-N_3$; 100(85); 71(40); 69(35); 59(60), metastable: 82.4(155 $\xrightarrow{-42}$ 113)].

Catalytic hydrogenation of IV afforded V. The mass spectrum of V is identical (within experimental error) to methyl ristosaminide isolated from ristomycin[4].

Benzoylation of V in aqueous tetrahydrofurane resulted in methyl N-benzoylristosaminide (VI). In t.l.c. V and VI proved to be identical with methyl 2,3,6-trideoxy-3-amino-α-L-ribo-hexopyranoside, prepared by the methanolysis of ristomycin, and its N-benzoyl derivative, respectively [$R_{f(V)}$ 0.76 (isopropanol: water: 25 % NH_4OH = 6:2:1), $R_{f(VI)}$ 0.54 (abs. benzene:methanol = 85:15)].

Acid hydrolysis of VI gave crystalline VII which on the basis of mixed m.p., specific rotation, t.l.c. and i.r. spectrum [m.p. 126-128 °C (from ethanol), lit.[4] m.p. 131-133 °C (from water), mixed m.p. 128-130 °C; $[\alpha]_D^{23}$ -10° (c 0.7, ethanol) after 10 min., lit.[4] $[\alpha]_D^{20}$ -14 $\longrightarrow$ -11° (c 1, ethanol) after 10 min.; t.l.c. R_f 0.25 (abs. benzene·methanol = 85·15), lit.[4] R_f 0.25 (abs. benzene:methanol = 85 15), R_f 0.92 (chloroform:methanol = 4:1)] was found to be identical with N-benzoylristosamine[4] obtained from methyl ristosaminide of natural source.

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