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THE STRUCTURES OF ANTIBIOTICS YL-704 A AND B

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In our screening studies for new antibiotics produced by streptomycetes, a new series of basic macrolide complex, numbered YL-704, was isolated from the solvent extract of the culture filtrate of Streptomyces platensis var. sp. MCRL 0388. Isolated YL-704 complex was constituted by several antibiotics and the structures of major two components (YL-704 A and B) were clearly determined.

The properties of two antibiotics were as follows: YL-704 A (I), $C_{43}H_{71}NO_{15}$ (C 61.26, H 8.38, N 1.88%, MW. 841), mp. 122-3°C, $[\alpha]_D^{21}$-50.2°(C 1, $CHCl_3$), UV*1: 232.5 mμ(log ε 4.45), IR*1: 3450, 2720, 1742, 1736, 1655, 1620 cm^{-1}, NMR*2: 9.68(1H, CHO), 5.50-6.80(4H, m, olefine), 3.57(3H, s, OCH_3), 2.54 (6H, s, $N(CH_3)_2$), 0.90-1.35(24H, $8CH_3$), YL-704 B (II), $C_{41}H_{67}NO_{15}$ (C 60.89, H 8.33, N 1.71%, MW. 813), mp. 131-2°C, $[\alpha]_D^{21}$-42.1° (C 1, $CHCl_3$), UV: 232.5 mμ(log ε 4.37), IR: 3450, 2725, 1745, 1738, 1670, 1640 cm^{-1}, NMR: 9.68(1H, CHO), 5.50-6.85(4H, m, olefine), 3.57(3H, s, OCH_3), 2.54(3H, s, $N(CH_3)_2$), 0.90- 1.35 (21H, $7CH_3$). Both antibiotics gave diacetates; diacetyl YL-704 A (III), $C_{47}H_{75}NO_{17}$, m/e 925 (M^+), mp. 114-5°C and diacetyl YL-704 B (IV), $C_{45}H_{71}NO_{17}$, m/e 897 (M^+), mp. 116-8°C, respectively. In NMR spectra, new signal at 2.03

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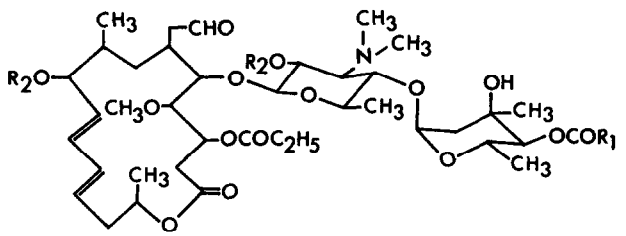
*1 UV and IR were measured in EtOH and in Nujol, respectively.

*2 Measured in $CDCl_3$, δ(ppm), 100 MHz.

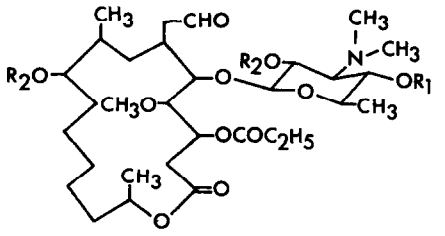
(6H, s) was observed in the both of III and IV.

The catalytic hydrogenation of I and II afforded tetrahydro derivatives V (mp. 103-4°C) and VI (mp. 99-100°C), respectively and by the mild hydrolysis, two kinds of acylsugar were isolated as the methyl glycoside. They were entirely identical with methyl 4-O-isovaleryl mycaroside and methyl 4-O-propionyl mycaroside, respectively, from their gas-chromatographic behavior and mass-spectrometric fragmentation pattern.[1,2]

From the solvent extract of the hydrolysates of V and VI, the same basic substance (VII, $C_{31}H_{55}NO_{11}$, mp. 90-1°C) was obtained. Acetylation of VII afforded triacetate (VIII), $C_{37}H_{61}NO_{14}$, m/e 743 (M^+), mp. 96-7°C, UV: end absorption, IR: 3500, 2730, 1740-20 cm^{-1}, and further strong acid hydrolysis of VII yielded an amino-sugar, $C_8H_{17}NO_4$, which was identified as mycaminose.[3]



I, R_1:$CH_2CH(CH_3)_2$, R_2:H
II, R_1:CH_2CH_3 , R_2:H
III, R_1:$CH_2CH(CH_3)_2$, R_2:$COCH_3$
IV, R_1:CH_2CH_3 , R_2:$COCH_3$
IX, R_1:$CH_2CH(CH_3)_2$, R_2:$COCH_2CH_3$



V, R_1:4-O-isovalerylmycarose, R_2:H
VI, R_1:4-O-propionylmycarose, R_2:H
VII, R_1:R_2: H
VIII, R_1:R_2: $COCH_3$

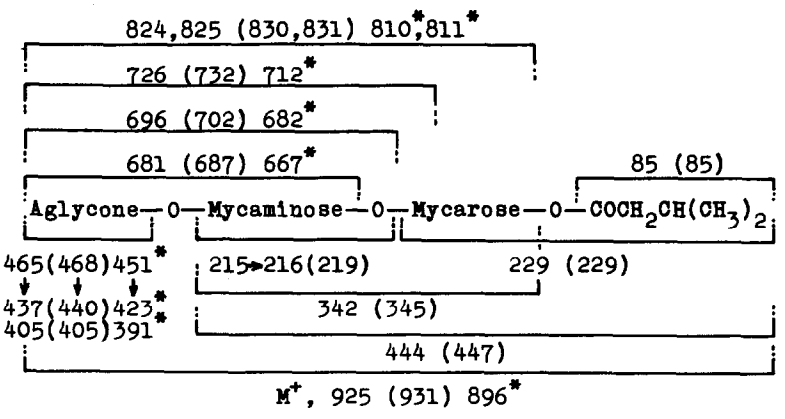
The physicochemical and biochemical properties of antibiotics I and II were very similar to leucomycin A_3 ($C_{42}H_{69}NO_{15}$; 3-$OCOCH_3$ in I)[4] and the compound (VIII) resembled demycarosyl tetrahydroleucomycin A_1-tetraacetate ($C_{36}H_{59}NO_{14}$; 3-$OCOCH_3$ in VIII)[5] in various behaviors.

To make sure the difference between YL-704 and leucomycin series, precise analyses of mass spectra were studied by deuterium labelling experiment and high resolution mass spectrometry.

For example, fragmentation patterns of III and its labelling compound (di-(trideuteroacetyl)-I) were summarized in Scheme 1. The fragmentation pattern of III was identical with that of diacetyl leucomycin A_3 in the sugar part, but the fragment involving the aglycone portion in III shifted by 14 mass units to higher region. The composition of the predominant fragments of III were finally established by high resolution mass spectrometry.[6)]

On tetrahydro-derivative (VIII), the fragment peaks due to the aglycone portion were reasonably shifted by 4 mass units comparing with those of III.

Scheme 1**



**Fragmentation pattern reflecting bond-sequence in diacetyl-YL-704 A (III). The alabic numbers are m/e in III, and the parenthesized ones show m/e in deuterium labelling compound. The asterisked numbers indicate m/e of the corresponding fragments in diacetyl leucomycin A_3, and the others are identical with those of III.

The methylene-unit difference between I and leucomycin A_3 was finally ascribed to the nature of the substituent at C_3-position from spectral studies.

Therefore, dipropionyl YL-704 A (IX), $C_{49}H_{79}NO_{17}$, mp. 111-2°C, $[\alpha]_D^{22}$-69.0° (C 1, $CHCl_3$), UV: 232-3 mμ (log ε 4.50), IR: 3500, 2710, 1750, 1730, 1712, 1680, 1655 cm^{-1}, NMR: 9.64(1H, CHO), 4.85-6.90(4H, m, olefine), 3.43(3H, s, OCH_3), 2.36(6H, s, $N(CH_3)_2$), MS: m/e 953 (M^+), 925 (M-28), 724, 479, 458, 451, 405, 356, 230, 229 and 143, was prepared and compared directly with the sample of tripropionate of leucomycin A_1 ($C_{40}H_{67}NO_{14}$; 3-OH in I).[5] Consequently, the both samples were completely identical with each other, and this fact indicated that the stereochemical problem of I was seemed to be the same as that of leucomycin series. The direct comparison was also done on the propionates of demycarosyl compounds derived from tetrahydro YL-704 A (V) and tetrahydro leucomycin A_1.

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6) Detailed results on high resolution mass spectrometry will be published elsewhere.