STUDIES ON THE MACROLIDE ANTIBIOTIC YL-704 COMPLEX. III

THE STRUCTURES OF NEW MACROLIDE ANTIBIOTICS YL-704 A_1 AND B_1

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New macrolide antibiotics YL-704 A_1 and B_1 were isolated from the culture broth of *Streptomyces platensis* subsp. *malvinus* MCRL 0388 and the structures of them were elucidated with physicochemical microanalyses including the mass spectrometry of their derivatives and the chemical degradation studies. The structure of the sixteen-membered aglycone was the same in YL-704 A_1 and B_1, while, the acyl groups of the sugar were isovaleryl and propionyl, respectively. Finally, dipropionyl YL-704 A_1 was entirely identified with tripropionyl leucomycin A_1.

The isolation of the basic macrolide antibiotic YL-704 complex produced by *Streptomyces platensis* subsp. *malvinus* MCRL 0388 was reported in the previous paper.[1] Two major components YL-704 A_1(**1**) and B_1(**2**) were studied to elucidate the structures,[2] and in this paper the details are described.

(**1**) and (**2**) showed similar physicochemical properties. Their IR spectra suggested the presence of hydroxyl (3450 cm^{-1}), aldehyde (2720 cm^{-1}), lactone and ester carbonyl (1742, 1736 cm^{-1}), double bonds (1655, 1620 cm^{-1}). The UV maximum absorption at 232.5 nm (log ε 4.45, EtOH) showed the chromophore of an α, β, γ, δ-unsaturated alcohol in (**1**) and also 232.5 nm (log ε 4.37, EtOH) in (**2**). In the PMR spectrum of (**1**) measured in $CDCl_3$, the presence of eight C-methyl (24H, 0.90~1.35 ppm), one N-dimethyl (6H, s, 2.54 ppm), one O-methyl (3H, s, 3.57 ppm), four olefinic (4H, m, 5.50~6.80 ppm) and one aldehydic (1H, s, 9.68 ppm) protons was assigned. The semicarbazone (**3**) of (**1**) showed the triplet (J=5.8 Hz, $-CH_2-CH=N-$) at 7.35 ppm in stead of an aldehydic proton of (**1**) in the PMR, it was found that a primary aldehyde was present in (**1**). (**2**) showed the very similar PMR spectrum except one less C-methyl group than (**1**).

All these properties were analogous to leucomycins,[3] but lacked the acetyl methyl signal at 2.22 ppm in PMR and the strong absorption at 1235 cm^{-1} in IR of leucomycin A_3 group.

IR and PMR spectra of (**1**) and (**2**) were depicted in Figs. 1 and 2.

On the total acetylation, (**1**) and (**2**) were estimated to give each diacetate and their molecular weights of acetates were measured with the mass spcetrometry. *m/e* 925(M^+) for diacetyl YL-704 A_1(**4**) and *m/e* 897(M^+) for diacetyl YL-704 B_1(**5**) showed 14 mass units difference from *m/e* 911(M^+) for diacetyl leucomycin A_3.[3b] Their bis (trideuteroacetyl) derivatives shifted reasonably to *m/e* 931, 903 and 917, respectively.

From both hydrolyzates of (**1**) and (**2**) with 6 N hydrochloric acid, one basic sugar was isolated to identified as mycaminose hydrochloride (**6**) by m.p., IR and TLC comparing to the authentic sample from leucomycins.[3]

Fig. 1. IR spectra of YL-704 A_1 (1) and B_1 (1) (Nujol).

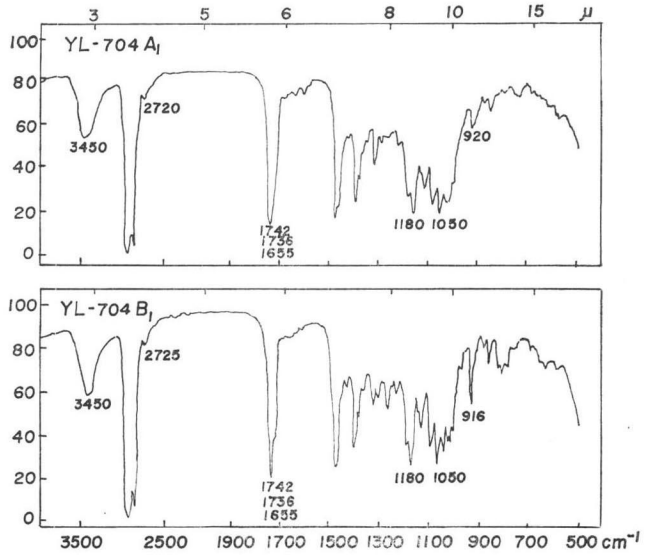
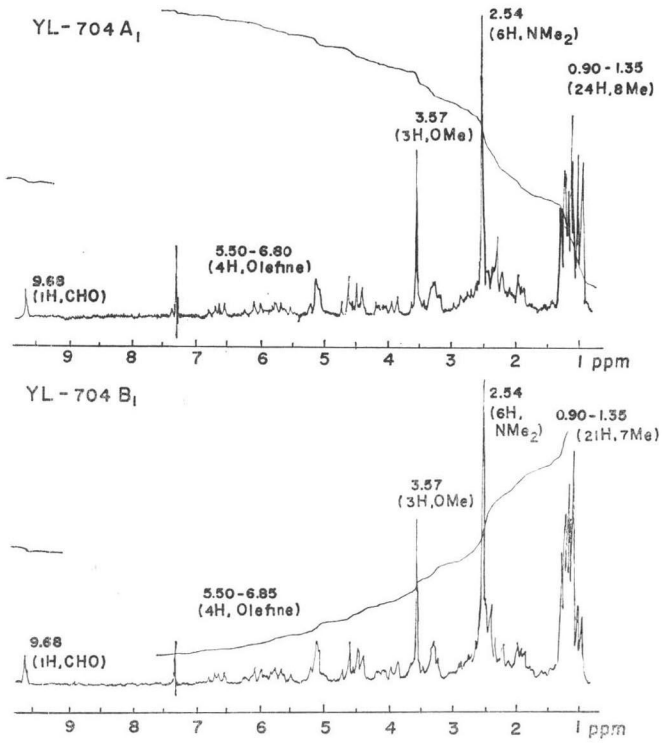


Fig. 2. PMR spectra of YL-704 A_1 (1) and B_1 (2).

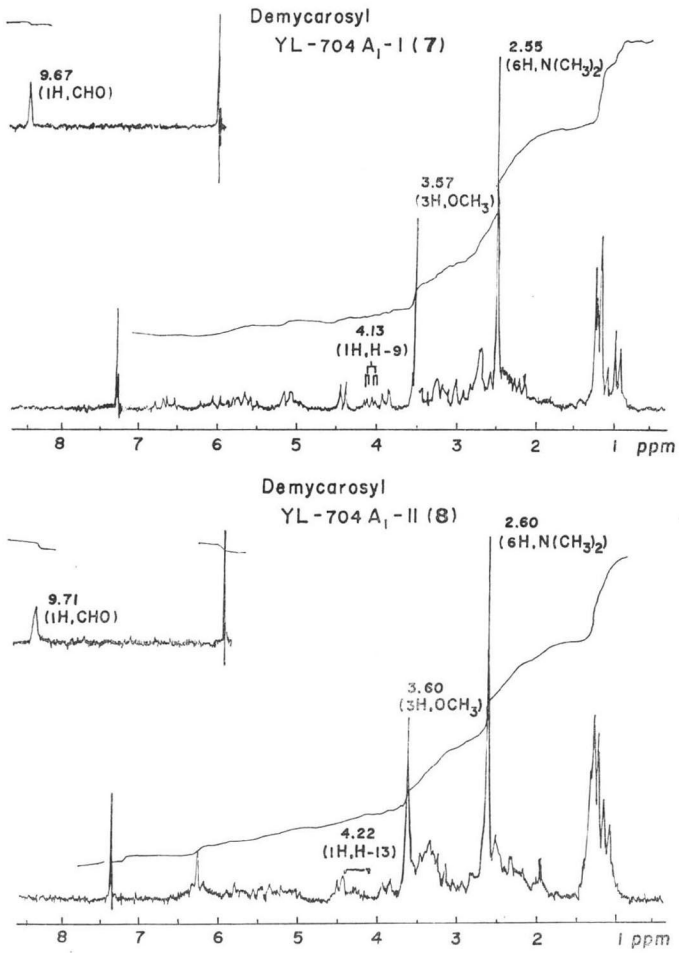


On mild acid hydrolysis of (1), two basic substances were obtained, following silica-gel column chromatography and further recrystallization from benzene. The first crystal, demycarosyl YL-704 A_1 II (8)* showed m.p. 185°C and the UV maximum at 235 nm (log ε 4.22), and the second, demycarosyl YL-704 A_1 I (7)* which was recrystallized from benzene-*n*-hexane showed

* The name of demycarosyl was dependent on the notation presented by OMURA and coworkers.[3]

m.p. 128~129°C and the UV maximum at 232 nm (log ε 4.25). Comparing the PMR between them, (**8**) showed the olefinic confused multiplet at 6.00~6.40 ppm and a broad signal of H-13 at 4.22 ppm, otherwise, (**7**) showed the same olefinic pattern and the same double doublet of H-9 (J=10, 3Hz) at 4.13 ppm, as (**1**). Owing to the mass spectra of their acetates, the molecular ion peak of the acetate (**9**, M^+ *m/e* 739) of (**7**) was identical with the acetate of (**8**) and larger by 14 mass units than triacetyl demycarosyl leucomycin A_3[3] (M^+, *m/e* 725), and their fragmentation patterns were closely related. Consequently, (**8**) was estimated to be the 13-hydroxy allylic rearranged isomer of (**7**). PMR spectra of (**7**) and (**8**) were illustrated in Fig. 3.

Fig. 3. PMR spectra of demycarosyl YL-704 A_1-I (7) and demycarosyl YL-704 A_1-II (8).



From the neutral extract of mild acid hydrolysis of (**1**), an acyl sugar was isolated as the methyl glycoside. It was estimated to be methyl 4-O-acyl mycaroside from the PMR and the mass specrometry, and identified with authentic methyl 4-O-isovaleryl mycaroside (**10**)[3] obtained from leucomycin A_3.

The methyl glycoside from (**2**) was determined to be methyl 4-O-propionyl mycaroside (**11**) by its PMR and mass spectral comparison to the methyl glycoside from leucomycin A_6.[3c]

Catalytic hydrogenation of (**1**) with palladium-carbon in ethanol gave tetrahydro YL-704 A_1 (**12**)

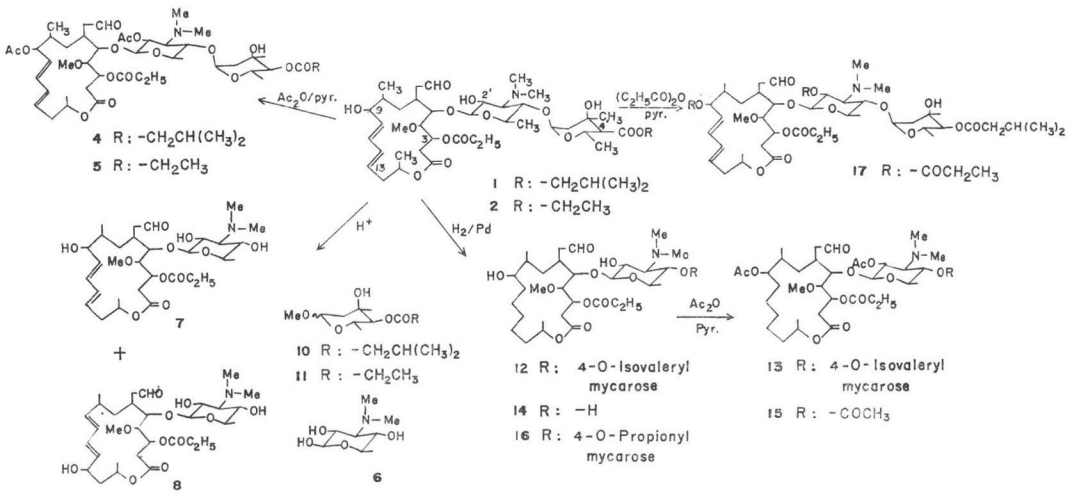
with only UV end absorption. The diacetate (**13**) of (**12**) showed the reasonable M^+ *m/e* 929. Mild acid hydrolysis of (**12**) afforded only one basic substance, tetrahydro demycarosyl YL-704 A_1 (**14**). Mass spectrometry of triacetate (**15**, M^+ *m/e* 743) of (**14**) supported tetrahydroacetyl aglycone portion (AGL^+, *m/e* 469) and diacetyl mycaminose portion (*m/e* 258).

From the hydrolyzate of tetrahydro YL-704 B_1 (**16**) which was obtained from (**2**) by the same procedure of (**12**), the tetrahydro demycarosyl derivative was the same as to (**14**) by m.p., IR and PMR, whose acetate showed the identical mass spectrum to (**15**).

At this point, the aglycone portion of (**1**) and (**2**) was the same structure, and had one more methylene unit comparing to the aglycone of leucomycin A_3. That is, the propionyloxy function in the aglycone of (**1**) and (**2**) was found to take place to the acetyloxy function of leucomycin A_3. On the alkaline treatment of (**14**), a volatile fatty acid was isolated and detected to be propionic acid. The acyl group in mycarose moiety was isovaleroyl in (**1**) as in leucomycin A_3, in (**2**) it was propionyl as in leucomycin A_6.

The whole structures of (**1**) and (**2**)* and their reaction products were showed in Chart 1.

Chart 1. Structures of YL-704 A_1(**1**) and B_1(**2**) and their reaction products.



The relationship between YL-704 and leucomycin was confirmly obtained by the total propionylation. Dipropionyl YL-704 A_1 (**17**) was entirely identical with the tripropionyl leucomycin A_1 (**18**) by the m.p., IR (Fig. 4), PMR and mass spectrometry.

Mass spectra of (**4**) and (**5**) were depicted in Figs. 5 and 6, and their mass spectrometry analyses were showed by the diagnostic fragmentation pattern. Precise analyses of them were studied by the deuterium labelling experiments and the high resolution mass spectrometry. Fragmentation pattern of (**4**) and (**5**), and the labelling compound bis (trideuteroacetyl) YL-704 A_1 (**19**) were summarized in Fig. 7.

The middle region of the spectra (*m/e* 300~500) is very important and diagnostic, *e.g.*, in (**4**) the fragment peaks of aglycone (AGL^+, *m/e* 465), AGL^+– CO (*m/e* 437), AGL^+– CH_3COOH (*m/e* 405), AGL^+– CH_3COOH – CH_3CH_2COOH (*m/e* 331), acyldisaccharide (ADS^+, *m/e* 444) and disaccharide (*m/e* 342) show the constitution of the antibiotic.

* YL-704 B_1 (**2**) was found to be identical with SF-837[4] and espinomycin I.[5]

Fig. 4. IR spectra of dipropionyl YL-704 A_1(17) and tripropionyl leucomycin A_1 (18).

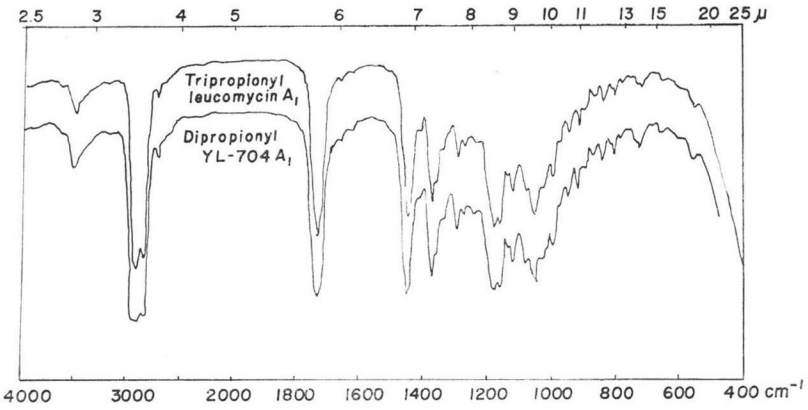


Fig. 5. Mass spectrum of diacetyl YL-704 A_1 (4).

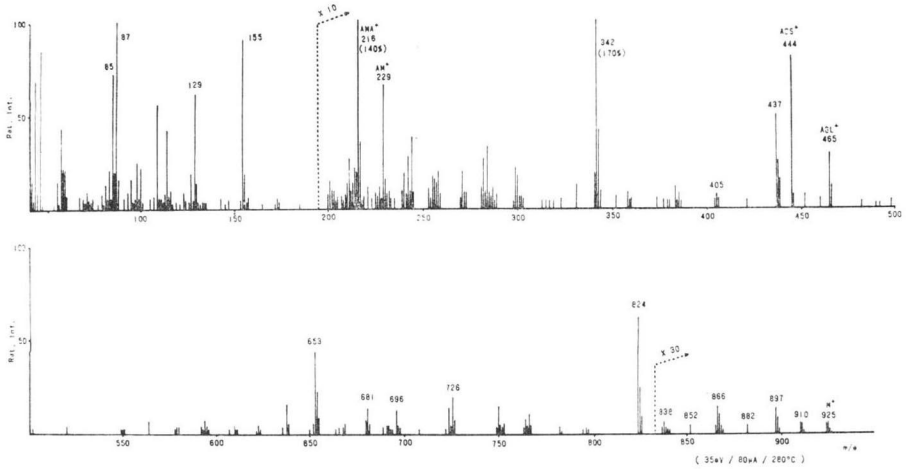


Fig. 6. Mass spectrum of diacetyl YL-704 B_1 (5).

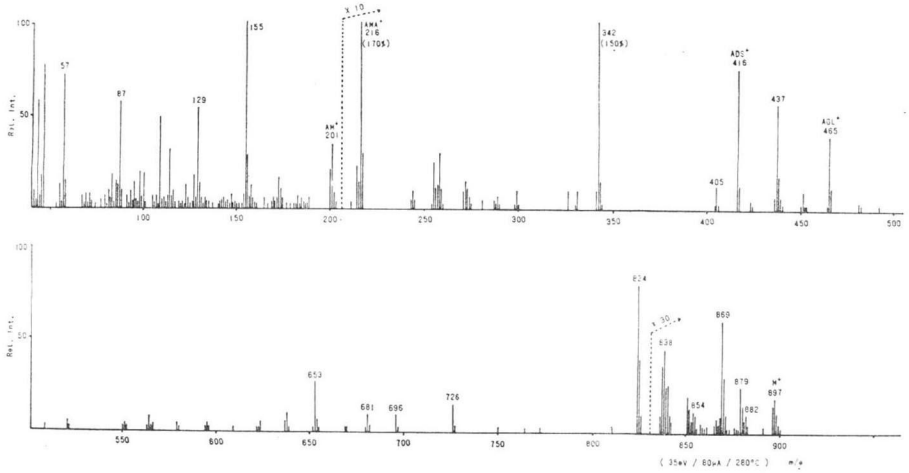


Fig. 7. Diagnostic fragmentations of diacetyl YL-704 A_1 (**4**, $R_1=-CH_2CH_3$, $R_2=-CH_2CH(CH_3)_2$), bis(trideuteroacetyl)YL-704 A_1 (**19**, in parenthese), diacetyl-YL-704 B_1* (**5**, $R_1=-CH_2CH_3$, $R_2=-CH_2CH_3$) and diacetyl leucomycin A_3**($R_1=-CH_3$, $R_2=-CH_2CH(CH_3)_2$).

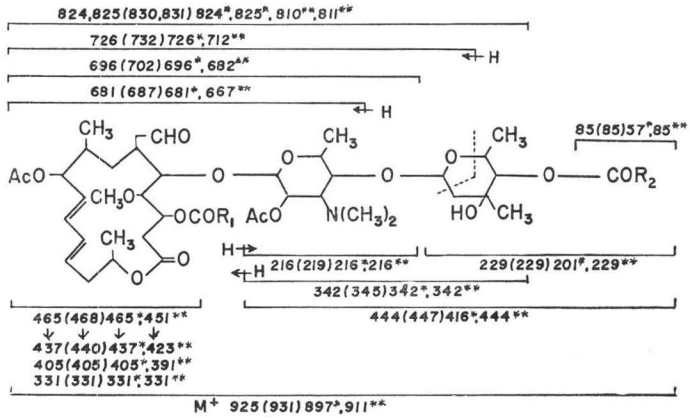


Table 1. High resolution mass spectrometry of predominant peaks of diacetyl YL-704 A_1 (**4**).

Obsd. Mass	Calcd. Mass	Error (mmu)	Formula
925.5048(M^+)	.5035	+1.3	$C_{47}H_{75}NO_{17}$
866.4907 (M-59)	.4902	+0.5	$C_{45}H_{72}NO_{15}$
726.3715	.3701	+1.4	$C_{36}H_{56}NO_{14}$
696.3589	.3595	−1.4	$C_{35}H_{54}NO_{13}$
653.3787	.3775	+1.2	$C_{34}H_{55}NO_{11}$
465.2471	.2488	−1.7	$C_{25}H_{37}O_8$
444.2572	.2597	−2.5	$C_{22}H_{38}NO_8$
437.2534	.2539	−0.5	$C_{24}H_{37}O_7$
342.1948	.1917	+3.1	$C_{17}H_{28}NO_6$
331.1935	.1909	+2.6	$C_{20}H_{27}O_4$
229.1423	.1440	−1.7	$C_{12}H_{21}O_4$
216.1206	.1236	−3.0	$C_{10}H_{18}NO_4$

The fragmentation pattern of the sugar part of (**4**) was identical to diacetyl leucomycin A_3, but the fragments involving the aglycone portion of (**4**) shifted by 14 mass units to higher region comparing to diacetyl leucomycin A_3.

The composition of the predominant fragments of (**4**) were finally established by high resolution mass spectrometry (Table 1).

Even on the tetrahydro derivative (**13**), which showed the similar fragmentation pattern, the fragment peaks including the aglycone portion were reasonably shifted to *m/e* 929(M^+), 469(AGL^+), 441(AGL^+− CO), 409(AGL^+− CH_3COOH) by 4 mass units comparing with (**4**).

Mass spectrometry of the acetyl derivatives was more advantageous for the volatility of some multifunctional macrolides and for the regular fragmentation pattern, and the shift method between acetyl and trideuteroacetyl derivatives showed the good availability for the structural studies.

Experimental

General Method

Melting points are uncorrected. IR spectra were measured with a Hitachi IR 215 and EPI

32 spectrometer. UV spectra were measured with a Hitachi 323 spectrophotometer. NMR-^{1}H spectra were measured at 100 MHz with a JNM 4H-100 and a PS-100 spectrometer. Mass spectra were measured with a Hitachi RMU 7L high resolution mass spectrometer. High resolution mass spectra were measured with a CEC-21 110B high resolution mass spectrometer. Thin-layer chromatography was employed for the detection of the course of reactions and the purity of the products, developed over silica gel GF_{254}(Merck) and alumina(Woelm) with benzene-acetone system. The chromatograms were visualized by heating at 120°C after spraying 40% H_2SO_4.

YL-704 A_1 semicarbazone (**3**)

(**1**) (50 mg) was dissolved in 1 ml EtOH and added with 0.4 ml H_2O. To this solution, semicarbazide (20 mg) in 1 ml H_2O and 10 mg CH_3COONa were added. The reaction was carried out at 80°C by stirring for 20 minutes. After cooling 3 ml H_2O was poured into and extracted with ethylacetate under pH 8. The extract was washed with water, dried over Na_2SO_4 and concentrated to dryness. The residue was crystallized from ethylacetate-*n*-hexane. (Yield 42 mg). m.p. 96~98°C.

Anal. calcd. for $C_{44}H_{74}N_4O_{15}$: C 58.85, H 8.03, N 6.24
Found: C 58.66, H 8.12, N 6.22

IR(nujol) 2380, 1690 cm^{-1}. PMR$(CD_3)_2CO$ δ 7.35(1H, t, J=5.8 Hz. $-CH_2-C\underline{H}=N-$)

Diacetyl YL-704 A_1 (**4**)

YL-704 A_1 (100 mg, **1**) was dissolved in 2 ml pyridine and 2 ml acetic anhydride was added to the solution, the mixture was allowed to stand at room temperature overnight. The reaction mixture was poured into ice water, pH of the solution was adjusted to 8. After twice extracting with ethylacetate, the extract was washed with water and dried over Na_2SO_4, and then evaporated under reduced pressure to 2 ml. By adding *n*-hexane to the residual solution, the white precipitate was resulted, which was recrystallized from ethylacetate-*n*-hexane. Colorless prism of diacetyl YL-704 A_1 (98 mg) was produced. m.p. 116°C.

Anal. calcd. for $C_{47}H_{75}NO_{17}$: C 60.97, H 8.11, N 1.51
Found: C 60.96, H 8.17, N 1.53

UV(EtOH) 232.5 nm (log ε 4.46), IR(nujol) 3495, 2730, 1760, 1745, 1738, 1675, 1645, 1252 cm^{-1}. PMR$(CDCl_3)$ δ 2.03(6H, s, 2×CH_3CO-). $[\alpha]_D^{21}$—66.0°(*c* 1, $CHCl_3$).

Diacetyl YL-704 B_1 (**5**)

YL-704 B_1 (100 mg, **2**) was acetylated by the method such as diacetyl YL-704 A_1. Diacetyl YL-704 B_1 (**5**) was recrystallized from ethylacetate-*n*-hexane and afforded 96 mg colorless needles. m.p. 117~118°C.

Anal. calcd. for $C_{45}H_{71}NO_{17}$: C 60.20, H 7.91, N 1.56
Found: C 60.41, H 8.02, N 1.59

UV(EtOH) 232.5 nm (log ε 4.37), IR(nujol) 3495, 2735, 1765, 1748, 1738, 1670, 1635, 1255 cm^{-1}. PMR$(CDCl_3)$ δ 2.02(6H, s, 2×CH_3CO-). $[\alpha]_D^{21}$-60.1°(*c* 1, $CHCl_3$)

Mild acid hydrolysis of (**1**)

To 0.3 N hydrochloric acid (15 ml), 500 mg of (**1**) was added and stirred at 5°C for 24 hours. pH of mixture was adjusted to 4.0 and the neutral product was extracted with $CHCl_3$. Chloroform layer was washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. Aqueous layer was adjusted to pH 8 and the basic products were extracted with $CHCl_3$ which was washed with water, dried over Na_2SO_4 and evaporated to dryness.

Isolation of mycaminose (**6**) from hydrolyzate of (**1**)

One gram of (**1**) was refluxed in 6 N HCl (10 ml) for 2 hours. Extracts of the reaction mixture with 10 ml isopropanol (60°C) was concentrated to 1 ml and H_2O was added. Amino sugar in water was absorbed on Dowex-50 W (H-type, 1 g) column, eluted with 0.5 N HCl and the elutes was concentrated to paste. Further purification was done by passing through Sephadex LH-20 (40 ml, MeOH) and the elutes were evaporated to dryness. The residue was

recrystallized from H_2O-isopropanol. Colorless needles (72 mg) were obtained as mycaminose hydrochloride. m.p. 114~115°C.

Anal. calcd. for $C_8H_{17}NO_4 \cdot H_2O \cdot HCl$: C 39.10, H 8.20, H 5.70, Cl 14.43
Found: C 39.28, H 8.27, N 5.56, Cl 14.50

The isolated mycaminose hydrochloride was compatible with the authentic sample from leucomycins.

Demycarosyl YL-704 A_1-I (**7**) and -II (**8**)

The basic substances (345 mg) from the hydrolysates of (**1**) were chromatographed over silica gel (30 g) column (methylacetate-isopropanol-H_2O, 8:1:2) and separated to two compounds. Demycarosyl YL-704 A_1-I (**7**) was recrystallized from ethylacetate-*n*-hexane (Yield 125 mg) and demycorosyl YL-704 A_1-II (**8**) was done from benzene (Yield 105 mg). (**7**): m.p. 128~129°C.

Anal. calcd. for $C_{31}H_{51}NO_{11}$: C 52.22, H 7.21, N 1.96
Found: C 52.33, H 7.13, N 1.87

UV(EtOH) 232 nm (log ε 4.25). IR(nujol) 3420, 2715, 1735, 1725, 1660, 1630 cm^{-1}. PMR($CDCl_3$) δ 4.13(1H, d.d, J=11, 4.5 Hz, H-9).

(**8**): m.p. 185~187°C.

Anal. calcd. for $C_{31}H_{51}NO_{11}$: C 52.22, H 7.21, N 1.96
Found: C 52.28, H 7.19, N 2.05

UV(EtOH) 235 nm (log ε 4.18). IR(nujol) 3450, 2715, 1740, 1730, 1655, 1640 cm^{-1}. PMR($CDCl_3$) δ 4.22(1H, m, H-13).

Triacetyl demycarosyl YL-704 A_1-I (**9**)

Two hundreds mg of (**7**) was acetylated to triacetate by the above usual method, which was recrystallized from benzene-*n*-hexane as colorless prisms (Yield 180 mg). m.p. 96~97°C.

Anal. calcd. for $C_{37}H_{57}NO_{14}$: C 60.08, H 7.71, N 1.89
Found: C 60.22, H 7.63, N 1.87

M.W. 739 (M^+, *m/e*).UV(EtOH) 232 nm (log ε 4.21). PMR($CDCl_3$) δ 1.99(6H, s, 2×CH_3CO–), 2.01(3H, s, CH_3CO–).

Methyl 4-O-isovaleryl mycaroside (**10**)

The neutral product (120 mg) from acid hydrolysis of (**1**) was refluxed in the anhydrous 1% HCl–MeOH for 2 hours. The reaction mixture was concentrated and chromatographed over silica gel column (benzene-acetone, 20:1) and the anomers were separated each other.

α-Methyl 4-O-isovaleryl mycaroside: b.p. 120~123°C/4 mm. $[\alpha]_D^{21}$ −135° (*c* 0.1, $CHCl_3$).

Anal. calcd. for $C_{13}H_{24}O_5$: C 60.05, H 9.30
Found: C 60.11, H 9.23

β-Methyl 4-O-isovaleryl mycaroside: amorphous. $[\alpha]_D^{21}$ +15° (*c* 0.1, $CHCl_3$).

Methyl 4-O-isovaleryl mycaroside was identified with that from leucomycin A_3.

Methyl 4-O-propionyl mycaroside (**11**)

(**2**) (500 mg) was dissolved in 10 ml 0.3 N hydrochloric acid and allowed to stand at 5°C for 20 hours. The reaction mixture was extracted with chloroform, the extracts were washed with water, dried over Na_2SO_4 and concentrated to the paste. The residue was refluxed in 5 ml MeOH satd. 3.5% HCl for 2 hours. Methanol was evaporated, 10 ml water was added and neutralized with aqueous $NaHCO_3$. Chloroform extracts from the neutral solution were washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. The residual products were chromatographed over 15 g silica gel (benzene-acetone, 20:1). Fraction Nos. 11~14 and fraction Nos. 17~20 were α-methyl 4-O-propionyl mycaroside and β-anomer, respectively. For the further purification, α-anomer was distilled and β-anomer was recrystallized from ether-*n*-hexane.

α-Methyl 4-O-propionyl mycaroside: b.p. 99~101°C/2 mm.

Anal. calcd. for $C_{11}H_{20}O_5$: C 56.88, H 8.68
Found: C 56.95, H 8.62

$[\alpha]_D^{21}$ −153° (*c* 1, $CHCl_3$).

β-Methyl 4-O-propionyl mycaroside: m.p. 70~71°C

Anal. calcd. for $C_{11}H_{20}O_5$: C 56.88, H 8.68
Found: C 56.90, H 8.64

$[\alpha]_D^{21}$ +22° (*c* 1, $CHCl_3$)

Tetrahydro YL-704 A_1 (**12**)

Catalytic hydrogenation of (**1**) (1 g) was carried out with 200 mg palladium-carbon (5%) in ethanol; 1.9 mols hydrogen were absorbed after 6 hours. The reaction mixture was filtered and evaporated to dryness. The residue was recrystallized from ethylacetate-*n*-hexane. (**12**) (850 mg) was obtained as colorless prisms. m.p. 103~104°C.

Anal. calcd. for $C_{43}H_{75}NO_{15}$: C 61.12, H 8.95, N 1.66
Found: C 60.22, H 8.76, N 1.75

UV(EtOH) end absorption.

Diacetyl tetrahydro YL-704 A_1 (**13**)

The acetylation of (**12**) was carried out as above method with acetic anhydride and pyridine. Diacetate was obtained by recrystallization from ethylacetate and *n*-hexane. m.p. 109~111°C.

Anal. Calcd. for $C_{47}H_{79}NO_{17}$: C 60.76, H 8.55, N 1.51
Found: C 60.03, H 8.72, N 1.55

Tetrahydro demycarosyl YL-704 A_1 (**14**)

Eight hundreds mg of (**12**) was stirred in 5 ml 1 N HCl at room temperature for 1 hour. To the reaction mixture 10 ml H_2O were added and the pH was adjusted to 3.0 with saturated aqueous $NaHCO_3$. After the extraction of the solution with $CHCl_3$, the residual aqueous layer was readjusted to pH 8.0 and extracted with $CHCl_3$, which was washed with H_2O, dried with Na_2SO_4 and concentrated to dryness. The residue was recrystallized from ethylacetate-*n*-hexane (Yield 510 mg). m.p. 90~91°C.

Anal. calcd. for $C_{31}H_{55}NO_{11}$: C 60.34, H 8.99, N. 2.27
Found: C 59.43, H 8.79, N. 2.11

UV(EtOH) end absorption.

Triacetyl tetrahydro demycarosyl YL-704 A_1 (**15**)

Triacetate of (**14**) (200 mg) was obtained by the above usual method. Recrystallization of the acetate was done from ethylacetate-*n*-hexane (Yield 162 mg). m.p. 96~97°C.

Anal calcd. for $C_{37}H_{61}NO_{14}$: C 59.81, H 8.29, N 1.88
Found: C 58.58, H 8.17, N 1.82

UV(EtOH): end absorption. M.W. 743 (M^+, *m/e*)

Tetrahydro YL-704 B_1 (**16**)

YL-704 B_1 (**2**, 800 mg) was hydrogenated in 40 ml ethanol with 5% Pd-C; 1.95 mols of hydrogen were absorbed. Recrystallization from ethylacetate-*n*-hexane gave 650 mg tetrahydro YL-704 B_1 (**16**). m.p. 99~100°C.

Anal. calcd. for $C_{41}H_{71}NO_{15}$: C 60.27, H 8.76, N 1.72
Found: C 59.17, H 8.48, N 1.74

UV(EtOH): end absorption.

Tetrahydro demycarosyl YL-704 B_1 (**14**)

Hydrolysis of tetrahydro YL-704 B_1 was carried out as tetrahydro YL-704 A_1 and gave tetrahydro demycarosyl YL-704 B_1. m.p. 90~91°C.

Anal. calcd. for $C_{31}H_{55}NO_{11}$: C 60.34, H 8.99, N 2.27
Found: C 60.00, H 8.81, N 2.21

UV(EtOH) end

This compound was identical to tetrahydro demycarosyl YL-704 A_1 (**14**).

Dipropionyl YL-704 A_1 (**17**)

The reaction mixture of 200 mg (**1**), 2 ml pyridine and 2 ml propionic anhydride was allowed to stand at room temperature for 30 hours. The solution was poured into ice water, adjusted to pH 8 and extracted with chloroform. The extracts were washed with water, dried over Na_2SO_4 and evaporated to dryness. The residue was recrystallized from ethylacetate-*n*-hexane (Yield 188 mg). m.p. 112~113°C.

Anal. calcd. for $C_{49}H_{79}NO_{17}$: C 61.75, H 8.36, N 1.47
Found: C 61.66, H 8.31, N 1.41

$[\alpha]_D^{22}$ −69.0° (*c* 1, $CHCl_3$) M.W. 953 (M^+, *m/e*), UV(EtOH) 232~233 nm (log ε 4.50).

Tripropionyl leucomycin A_1 (**18**)

Leucomycin A_1 (200 mg) separated from leucomycin complex was propionylated in 2 ml pyridine with 2 ml propionic anhydride at room temperature for 3 days. The reaction mixture was treated as dipropionyl YL-704 A_1 (Yield 158 mg). m.p. 112~113°C.

Anal. calcd. for $C_{49}H_{79}NO_{17}$: C 61.75, H 8.36, N 1.47
Found: C 61.72, H 8.42, N 1.42

Bis(trideuteroacetyl) YL-704 A_1 (**19**)

The trideuteroacetyl derivative of (**1**) was prepared by the method as (**4**) with trideuteroacetic anhydride instead of acetic anhydride. (**4**) and (**19**) were identified on TLC of silica gel GF_{254} (Merck, benzene-acetone, 4:1).

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