CHEMICAL & PHARMACEUTICAL BULLETIN

Vol. 18, No. 8 August 1970

Regular Articles

[Chem. Pharm. Bull. 18(8)1501—1508(1970)]

UDC 547.918.02 : 576.8.098 : 615.33.011.5

Chemistry of Leucomycins. VIII.[1] Absolute Configuration of Leucomycin and Isoleucomycin

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(Received November 5, 1969)

Structural relationship between demycarosyl-leucomycin-A_3 proposed through X-ray crystallography by Hiramatsu, *et al.* and leucomycin-A_3 was examined, and it was found that the hydroxyl group at the C-9 position on lactone of the latter underwent allylic rearrangement being transferred to the C-13 position in the former on mild hydrolysis of the latter with dilute hydrochloric acid. On the other hand, isoleucomycin-A_3, whose hydroxyl group at the C-13 position was transferred from C-9 in leucomycin-A_3 without liberation of mycarose portion, was obtained by warm acid treatment of leucomycin-A_3. Configuration on the C-9 position was determined by applying the benzoate or Mills' rule to leucomycin-A_3 and, from the present and previously reported results, the absolute structure of leucomycin-A_3 was elucidated.

Leucomycins are macrolide antibiotics isolated from *Streptomyces Kitasatoensis* Hata by Hata, *et al.*,[3] in 1953. The eight analogs of leucomycin have already been isolated by Ōmura, *et al.*,[4–6] and their structural relationship has become clear.

The structure of one of the isomers of demycarosylleucomycin-A_3, mp 199—202° (**3**) obtained by hydrolysis of leucomycin-A_3 (**1**) with dilute hydrochloric acid (0.3N[7]) was determined by X-ray crystal structure analysis.[8] Comparison of the structure of **3** with that of **1** showed that the hydroxyl group at the C-9 on lactone in **1** appeared at the C-13 in **3** by

1) Part VII: S. Ōmura, M. Katagiri, T. Hata, M. Hiramatu, K. Kimura, and K. Naya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1402 (1968).
2) Location: *Shirokane, 5-9-1, Minato-ku, Tokyo*; *a) Nishinomiya, 662, Hyogo.*
3) T. Hata, Y. Sano, O. Ohki, Y. Yokoyama, A. Matsumae, and S. Ito, *J. Antibiotics*, **6**, 87 (1953).
4) S. Ōmura, M. Katagiri, H. Ogura, and T. Hata, *Chem. Pharm. Bull.* (Tokyo), **15**, 1929 (1967).
5) S. Ōmura, M. Katagiri, H. Ogura, and T. Hata, *Chem. Pharm. Bull.* (Tokyo), **16**, 1167 (1968).
6) S. Ōmura, M. Katagiri, and T. Hata, *Chem. Pharm. Bull.* (Tokyo), **16**, 1181 (1968).
7) S. Ōmura, M. Katagiri, T. Hata, M. Hiramatsu, T. Kimura, and K. Naya, *Chem. Pharm. Bull.* (Tokyo), **16**, 1402 (1968).
8) M. Hiramatsu, A. Furusaki, T. Noda, K. Naya, Y. Tomiie, I. Nitta, T. Watanabe, T. Take, and J. Abe, *Bull. Chem. Soc. Japan*, **40**, 2982 (1967).

allylic rearrangement during the hydrolysis.[7] Hydrolysis of **1** with dilute hydrochloric acid (0.2N HCl) was, however, found to give demycarosylleucomycin-A_3 (**2**), mp 145—146°, along with a minor amount of an isomer (**3**), having the same lactone skeleton as the parent molecule.

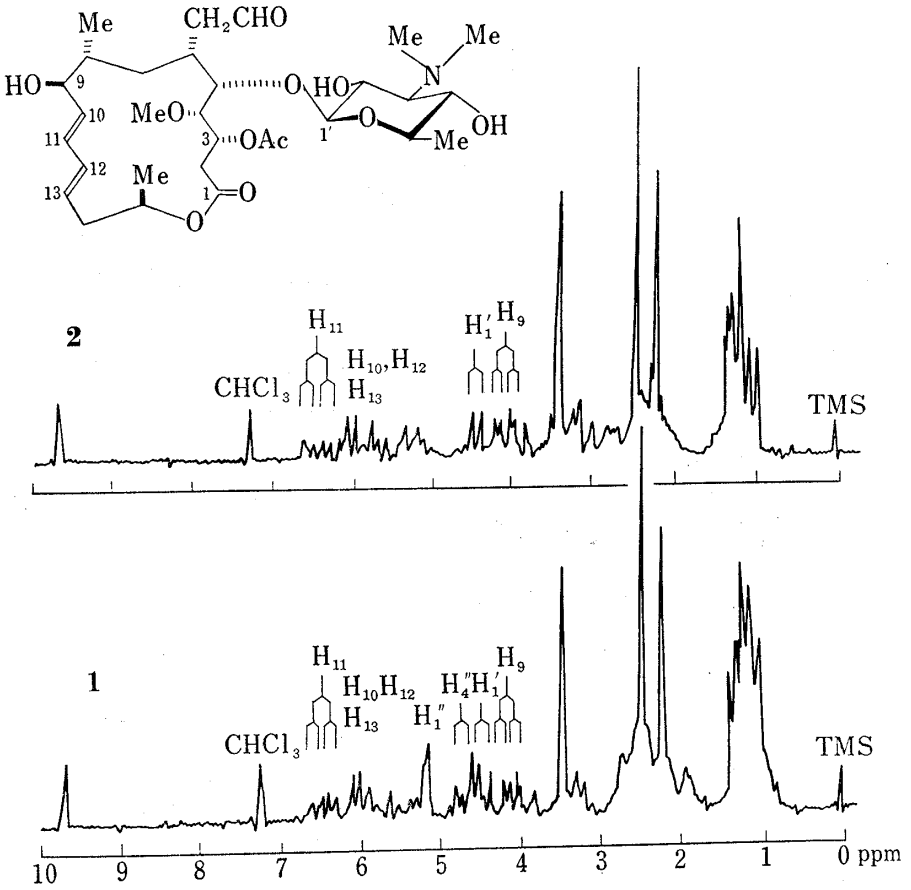


Fig. 1. 60 Mcps NMR Spectra of **1** and **2** in $CDCl_3$

It was deduced from the following nuclear magnetic resonance (NMR) spectra of **1** and **2** that no structural change had taken place in the lactone of **2** obtained by hydrolysis of **1** with dilute acid. As shown in Fig. 1, comparison of the 60-Mc NMR spectrum in $CDCl_3$ of **1** with that of **2** showed that these spectra are almost completely identical except for the absorption due to the protons in the mycarose portions; for example, the proton at anomer and the base proton of O-acyl group at C-4″ on mycarose. As previously reported,[6] absorption of the base proton of the hydroxyl group at C-9, which appeared as a double doublet because the proton at C-9 couples with the tertiary proton at C-8 and the olefinic proton at C-10 on lactone, was identical in **1** and **2**, and the pattern for olefinic proton region was also identical.

On the other hand, during the synthesis of various derivatives of leucomycin and a series of structural studies on leucomycin, we obtained isoleucomycin-A_3 (**4**), mp 180—182°, which seemed to be an isomer of **1**, during acid treatment of **1** under a mild condition (pH 2.0, 60°, 2 hr). It was very sparingly soluble in benzene. From comparison of the 100-Mc NMR spectrum of **4** in $CDCl_3$ with that of **3** in Fig. 2, it was found that the absorptions for protons due to mycaminose and lactone, especially the protons at the C-9 to C-13 position, were almost identical in **3** and **4**.

On the basis of the experimental data described above, the mycarose portion of **4** would not be cleaved under a mild acid treatment and **4** seems to be a compound in which the hy-

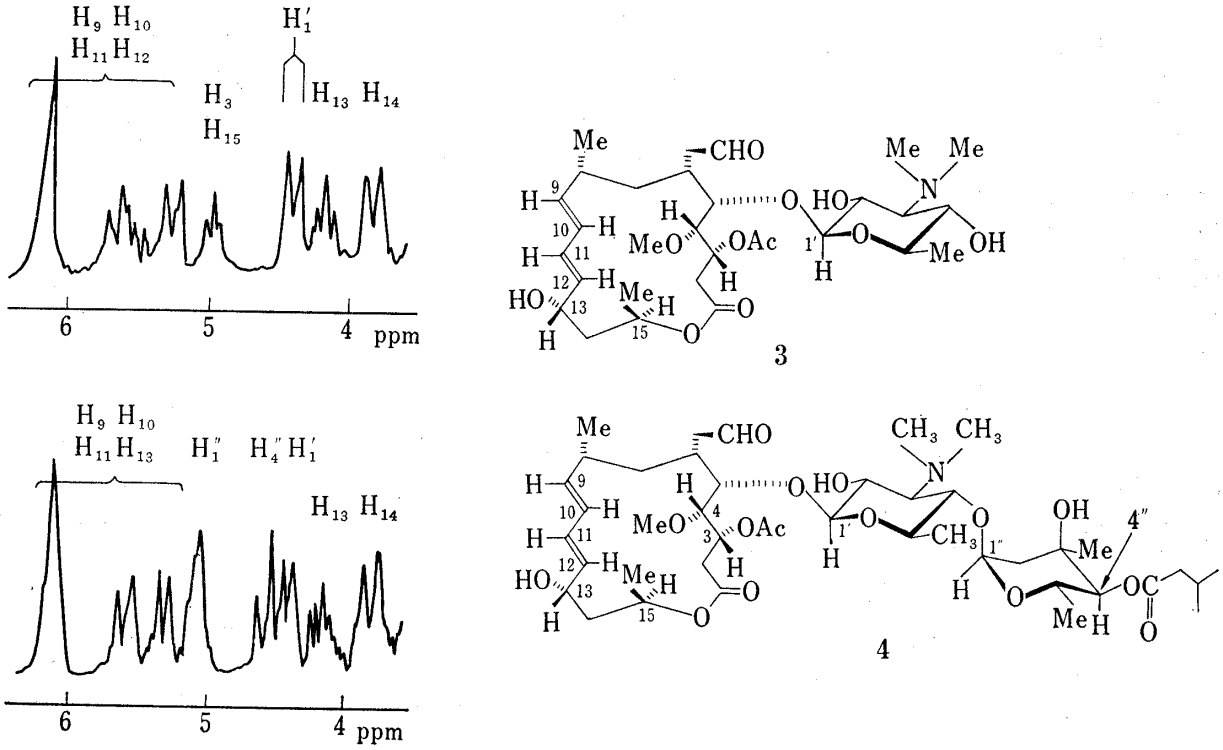


Fig. 2. 100 Mcps NMR Spectra of **3** and **4** in $CDCl_3$

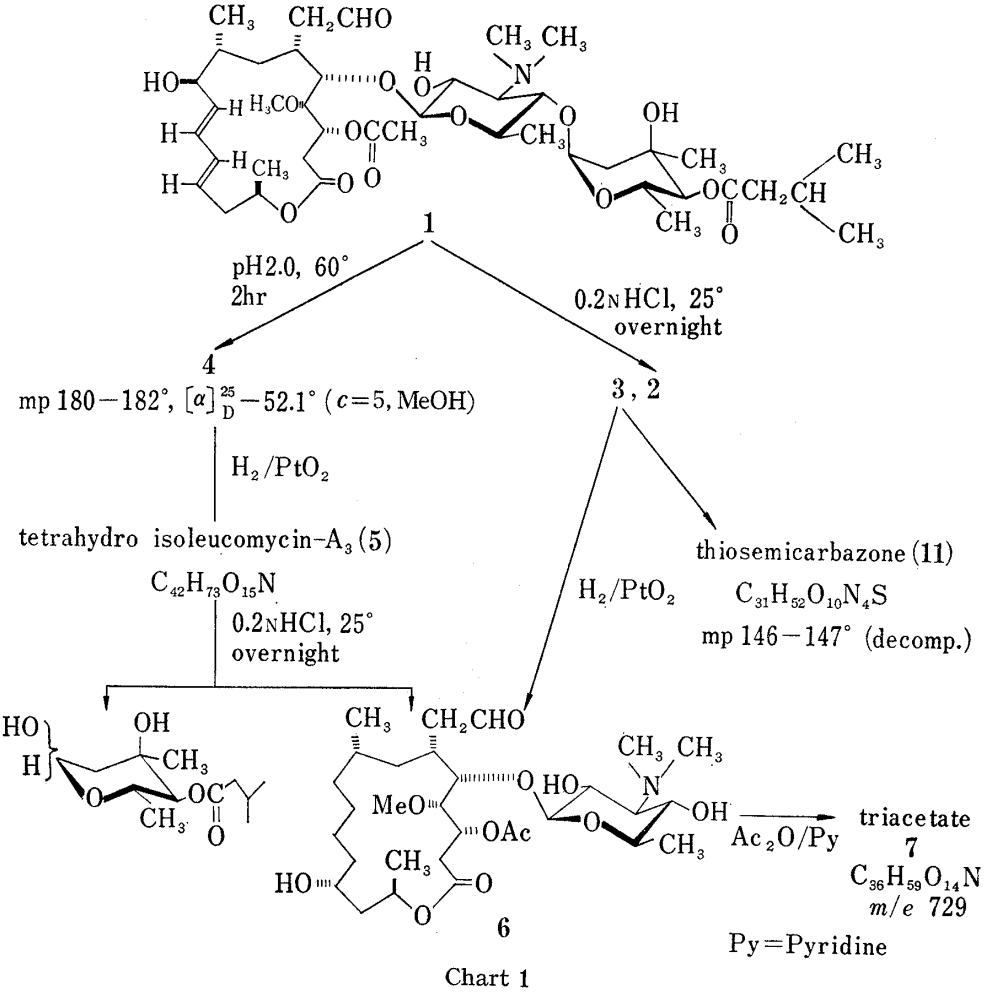


Chart 1

droxyl group at C-9 on lactone underwent allylic rearrangement to C-13, and this fact was confirmed by the following chemical procedures. As shown in Chart 1, **4** derived from **1** was catalytically hydrogenated over platinum oxide in ethanol to give tetrahydroisoleucomycin-A_3 (**5**) which was allowed to stand overnight at 25° in dilute hydrochloric acid (0.2N) and gave demycarosyl-tetrahydroisoleucomycin-A_3 (**6**). On the basis of thin-layer chromatography, specific rotation, and infrared spectrum, **6** was identical to the corresponding derivative from **3**. Further, **6** was acetylated in pyridine to give triacetyldemycarosylisoleucomycin-A_3 (**7**), which was also proved to be identical with that derived from **3** by mass spectrum (*m/e* 729). Therefore, it became clear that the structure on lactone in **4** was identical with that of **3**.

On the other hand, we elucidated by the following chemical methods that the hydroxyl group at C-9 in **2** obtained by hydrolysis of **1** with dilute hydrochloric acid, had not undergone allylic rearrangement. As shown in Chart 2, **2** was catalytically hydrogenated over platinum oxide in ethanol to give demycarosyl-tetrahydroleucomycin-A_3 (**9**), derived from **8** by a similar procedure, was identical to **9** derived from **3** on the basis of thin-layer chromatography, and specific rotation and infrared spectrum. Further, **2** and **3** were led to their respective thiosemicarbazones, **10** and **11**. In view of the above facts, since the presence of epimer of **3** has not been found in thin-layer chromatography it was elucidated that the hydroxyl group at C-9 on lactone in **2** had undergone allylic rearrangement stereo-specifically to C-13 in **3**.

From the fact[6] that the proton at the C-9 in NMR spectrum of **1** showed a double doublet at 4.05 ppm, it was found that the structural arrangement neighboring C-9 was shown as $-\overset{10}{CH}=\overset{9}{CH}-\overset{OH}{\overset{|}{\underset{|}{CH}}}-\overset{8}{CH}-$. In order to support the presence of the hydroxyl group situated at C-9 and of carbon skeleton from C-9 to C-13, the following Bayer–Villiger oxidation was applied

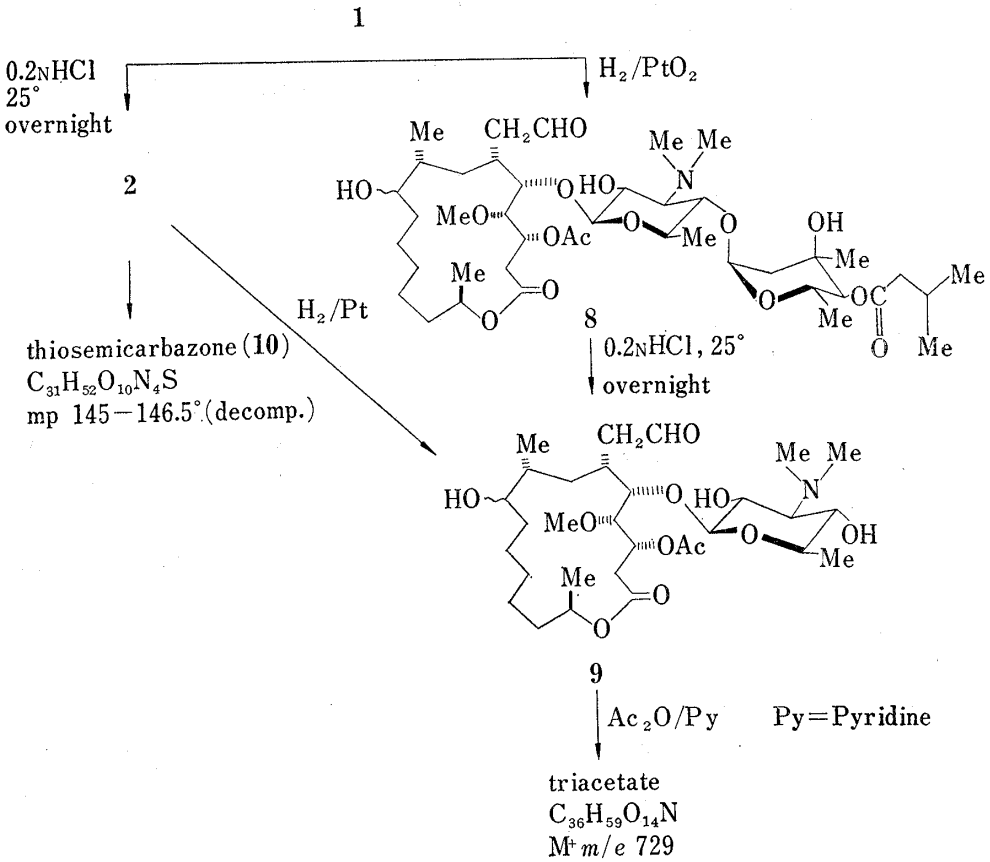


Chart 2

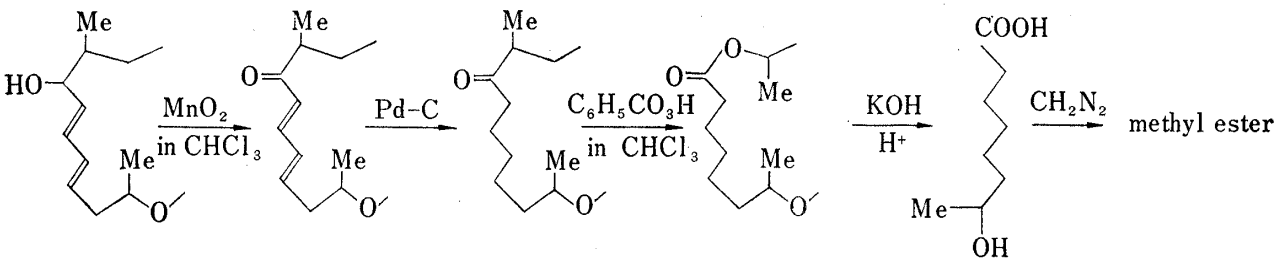


Chart 3

to the ketone mentioned below from **1**. Accordingly, as shown in Chart 3, **1** was oxidized with manganese dioxide in chloroform to give dehydroleucomycin-A_3 (**12**) in which the hydroxyl group at C-9 had been oxidized to carbonyl. The dehydro compound, **12** was then hydrogenated over palladium–charcoal giving tetrahydrodehydroleucomycin-A_3 (**13**), which was oxidized with a solution of perbenzoic acid and *p*-toluenesulfonate in benzene and pyridine, and the oxide thus obtained was hydrolyzed with alkaline solution to give an oily substance (**14**). The methyl ester of **14** was identified with that of 7-hydroxyoctanoic acid,[9] obtained by the synthesis, by gas liquid chromatography.

Finally, to determine the absolute configuration of the asymmetric carbon at C-9 on lactone, the benzoate or Mills' rule[10] was applied. Selective acetylation of the hydroxyl group at the C-2′ on mycaminose and not C-9 on lactone was attempted and 2′-monoacetylleucomycin-A_3 (**15**) was successfully obtained by acetylation of **1** with acetic anhydride in acetone.

As shown in Fig. 3, from comparison of the 60-Mc NMR spectra in $CDCl_3$ of **1** and **15**, it would be presumed that one hydroxyl group was acetylated, from the appearance of a singlet absorption at 2.02 ppm. Acetylation at C-2′ on mycaminose would be concluded from the following facts. The absorption at 4.05 ppm due to the proton at C-9 did not change and also, as shown in Table I, determination of $pK_{a'}$ for the related acetyl compound resulted in decrease of $pK_{a'}$ value by the introduction of an acetyl group at C-2′ such as **15**, II, and V. Compound **15** was used as the material for applying the benzoate or Mills' rule, as shown in Chart 4. 2′-Monoacetyl-tetrahydroleucomyc-inA_3 (**16**), obtained by catalytic hydrogenation of **15**, was derived to 3,5-dinitrobenzoate (**17**). It was found from the application of the benzoate rule that **16** and **17** belong to the R-system by comparison of their molecular rotation (−117°). **15** was also derived to the benzoate (**18**) by a similar method as above. It was found that from the difference of −308° in molecular rotation between **15** and **18**, they also belonged to the R-system. The absolute configuration on asymmetric carbon at C-9 on lactone could be concluded to have the R-system. Therefore, from the present results and the previously reported results on the glycosidic linkage and configuration of the diene

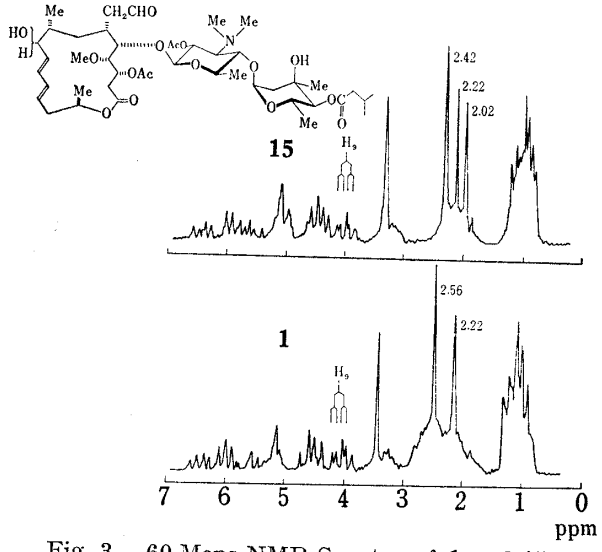


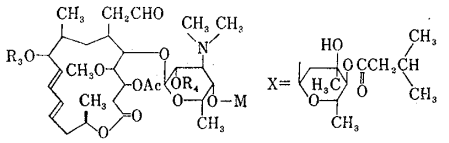
Fig. 3. 60 Mcps NMR Spectra of **1** and **15** in $CDCl_3$

9) J.T. Adams and C.R. Hauser, *J. Am. Chem. Soc.*, **66**, 1220 (1944).
10) J.H. Brewster, *Tetrahedron*, **13**, 106, (1961).

system, and from the X-ray crystallography, the absolute configuration of **1** has been revealed as represented in Chart 5.

Table I. pK_a' of Leucomycin-A_3 (**1**) and Its Related Compounds

Compound	M	R_3	R_4	pK_a' (50% EtOH) 5	6	7	8
Leucomycin-A_3 (**1**)	X	H	H			6.70	
2′-Monoacetylleucomycin-A_3 (**15**)	X	H	$COCH_3$		5.48		
2′, 9-Diacetylleucomcmycin-A_3 (III)	X	$COCH_3$	$COCH_3$		5.49		
9-Acetylleucomycin-A_3 (IV)	X	$COCH_3$	H			6.65	
Demycarosylleucomycin-A_3 (**2**)	H	H	H				7.80
Triacetyldemycarosylleucomycin-A_3 (V)	$COCH_3$	$COCH_3$	$COCH_3$	5.30			



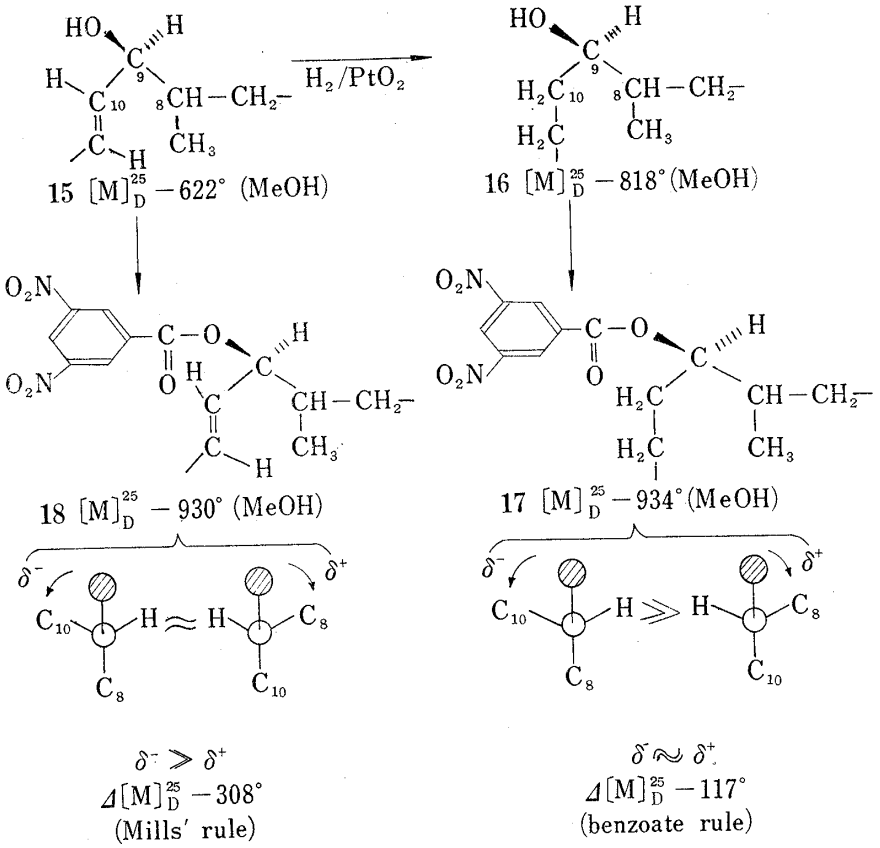


Chart 4

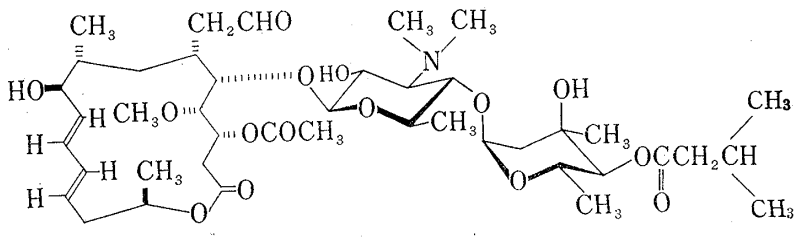


Chart 5. Absolute Configuration of **1**

Experimental

Demycarosylleucomycin-A_3 (2)——To 2 g of **1** was added 40 ml of 0.2N HCl, the mixture was adjusted to pH 2.0, and allowed to stand overnight at room temperature. Then the mixture was adjusted to pH 4.0 and extracted with three 20 ml portions of $CHCl_3$ removing isovalerylmycarose. The aqueous layer was adjusted to pH 8.0 with 0.1N NaOH and extracted with three 20 ml portions of $CHCl_3$. The extract was dried over anhyd. Na_2SO_4, filtered, and evaporated under a reduced pressure, leaving 400 mg of a white powder. To it was added 5 ml of benzene and the insoluble precipitate produced was filtered. Evaporation of the solvent from the filtrate left 360 mg of **2** as a white amorphous powder, mp 145—146°; $[\alpha]_D^{25}$ −27.4° ($c=5$, $l=1$, MeOH); UV λ_{max}^{MeOH} mμ ($E_{1cm}^{1\%}$) 232 (434). *Anal.* Calcd. for $C_{30}H_{49}O_{11}N$: C, 60.08; H, 8.24; N, 2.34. Found: C, 59.85; H, 8.23; N, 2.39. ORD ($c=0.4$, dioxan) $[\alpha]^{25}$ (mμ): 0° (260), 29.6° (273), −78.8° (300), −124° (314).

Demycarosylisoleucomycin-A_3 (3)——Through the same procedure as for **2**, 2 g of **1** was hydrolyzed with 40 ml of 0.2N HCl. To 460 mg of the white amorphous powder thus obtained was added 5 ml of benzene, the insoluble precipitate formed was collected, and washed with a small amount of benzene to obtain 85 mg (5.9%) of **3** as a white crystalline powder, mp 199—202° (decomp.); $[\alpha]_D^{25}$ −14.0° ($c=1$, $l=1$, $CHCl_3$); pK_a 7.80. *Anal.* Calcd. for $C_{30}H_{49}O_{11}N$: C, 60.08; H, 8.24; N, 2.34. Found: C, 60.5; H, 8.17; N, 2.28. ORD ($c=0.15$, dioxan): $[\alpha]^{25}$ (mμ): −0.28° (275), −20° (300), −267° (317) 33.3° (400).

Isoleucomycin-A_3 (4)——A solution of 5 g of **1** added to 250 ml of 0.1N HCl was adjusted to pH 2.0 and warmed for 2 hr at 60°. The reaction mixture was adjusted to pH 8.0 with 0.1N NaOH and extracted with three 40 ml portions of $CHCl_3$. The combined extract was dried over anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under a reduced pressure, leaving a white powder. It was crystallized from benzene to 170 mg (17%) of **4** as white needles, mp 180—182°, $[\alpha]_D^{25}$ −52.1° ($c=5$, $l=1$, MeOH); UV λ_{max}^{MeOH} mμ ($E_{1cm}^{1\%}$) 233.5 (339). *Anal.* Calcd. for $C_{42}H_{69}O_{15}N$: C, 60.92; H, 8.42; N, 1.69. Found: C, 61.11; H, 8.45; N, 1.78.

Tetrahydroisoleucomycin-A_3 (5)——A solution of 100 mg of **4** in 20 ml of EtOH was catalytically hydrogenated in the presence of 10 mg of PtO_2. The theoretical amount of H_2 was taken up in 2 hr. The solvent was removed from the filtrate in a rotary evaporator and left 95 mg (95%) of **5** as a white amorphous powder. $[\alpha]_D^{25}$ −86.0° ($c=0.5$, $l=1$, MeOH). *Anal.* Calcd. for $C_{42}H_{73}O_{15}N$: C, 60.63; H, 8.84; N, 1.64. Found: C, 60.59; H, 8.70; N, 1.68.

Demycarosyl-tetrahydroisoleucomycin-A_3 (6)——a) Through the same procedure as above 66 mg of **5** was hydrolyzed with 35 ml of 0.2N HCl. After removing isovalerylmycarose by extraction of the reaction mixture with $CHCl_3$ at pH 4.0, the aqueous layer was adjusted to pH 8.0 and extracted with $CHCl_3$. After drying the extract, the solvent was evaporated under reduced pressure, giving 29 mg (61%) of **6** as a white amorphous powder. $[\alpha]_D^{25}$ −27.6° ($c=1$, $l=1$, MeOH). *Anal.* Calcd. for $C_{30}H_{53}O_{11}N$; C, 59.70; H, 8.79; N, 2.32. Found: C, 59.82; H, 8.75; N, 2.33. Kieselgel G, thin-layer chromatography: *Rf* 0.64 (MeOH: $CHCl_3$=1:2).

b) A solution of 60 mg of **3** in 20 ml of EtOH was hydrogenated in the presence of 10 mg of PtO_2. Through the same procedure, 48 mg of **6** was obtained as a white amorphous powder. $[\alpha]_D^{25}$ −28.1 ($c=1$, $l=1$, MeOH). *Anal.* Calcd. for $C_{30}H_{53}O_{11}N$: C, 59.70; H, 8.79; N, 2.32. Found: C, 59.76; H, 8.78; N, 2.31. Kieselgel G, thin-layer chromatography: *Rf* 0.64 (MeOH:$CHCl_3$=1:2).

Triacetyl-demycarosyl-tetrahydroisoleucomycin-A_3 (7)——To a mixture of 25 mg of **6** in pyridine was added 0.1 ml of Ac_2O and the mixture was allowed to stand overnight. The solution was poured into ice-water with stirring and the produced precipitate was extracted with three 15 ml portions of $CHCl_3$. The combined extract was washed with a satud. $NaHCO_3$ solution and water, and dried over anhyd. Na_2SO_4. The solvent was removed in a rotary flash evaporator and left 20 mg (66%) of **7** as a white powder. Mass Spectrum *m/e* 729.

Tetrahydroleucomycin-A_3 (8)——A solution of 300 mg of **1** in 30 ml of EtOH was catalytically hydrogenated in the presence of PtO_2. About 2 moles of H_2 was absorbed in 2 hr. By the same procedure as above, 280 mg (94%) of **8** was obtained as a white powder. $[\alpha]_D^{25}$ −54.0 ($c=1.3$, $l=1$, $CHCl_3$). *Anal.* Calcd. for $C_{42}H_{73}O_{15}N$: C, 60.63; H, 8.84; N, 1.64. Found: C, 60.57; H, 8.62; N, 1.70.

Demycarosyl-tetrahydroleucomycin-A_3 (9)——a) A solution of 160 mg of **2** in 15 ml of EtOH was catalytically hydrogenated in the presence of 36 mg of PtO_2. The theoretical amount of H_2 was taken up in 2 hr, giving 110 mg (68%) of **9** as a white powder. $[\alpha]_D^{25}$ −19.7° ($c=0.95$, $l=1$, EtOH). *Anal.* Calcd. for $C_{30}H_{53}O_{11}N$: C, 59.70; H, 8.79; N, 2.32. Found: C, 59.5; H, 8.75; N, 2.30. Kieselgel G, thin-layer chromatography: *Rf* 0.60 ($CHCl_3$:MeOH=2:1).

b) By a similar procedure as above, 200 mg of **8** was hydrolyzed with 0.2N HCl to obtain 140 mg of **9** as a white amorphous powder. $[\alpha]_D^{25}$ −19.7° ($c=0.95$, $l=1$, EtOH). *Anal.* Calcd. for $C_{30}H_{53}O_{11}N$: C, 59.70; H, 8.79; N, 2.32. Found: C, 59.52; H, 8.75; N, 2.32. Kieselgel G, thin-layer chromatography: R_f 0.60 ($CHCl_3$:MeOH=2:1).

Demycarosylleucomycin-A_3 Thiosemicarbazone (10)——To a solution of 117 mg of demycaro compound (**2**) in 5 ml of EtOH was added 8 mg of thiosemicarbazide. The solution was refluxed for 4 hr and the solvent was evaporated under a reduced pressure. The residue was added with 2 ml of water, the mixture was

warmed for some time, and 150 mg of an amorphous precipitate was obtained. It was crystallized from 5 ml of EtOH to 58 mg of **10** as colorless needles. mp 145—146.5° (decomp.). *Anal.* Calcd. for $C_{31}H_{52}O_{10}N_4S$: C, 55.52; H, 7.64; N, 8.36. Found: C, 55.42; H, 7.85; N, 7.90. NMR ($CDCl_3$)τ: 9.14 (3H, doublet, J=5 cps, C-8 CH_3), 8.86 (5H, doublet, J=5 cps, C-5′ CH_3, C-15 CH_3), 2.81 (1H, triplet, J=5.5 cps, $-CH_2-CH{=}N-NH-$).

Demycaroslylisoleucomycin-A_3 Thiosemicarbazone (11)——A solution of 110 mg of isodemycaro compound (**3**) in 5 ml of EtOH added with 16 mg of thiosemicarbazide was refluxed for 4 hr and the same procedure as above gave 40 mg of thiosemicarbazone (**11**) as colorless needles, mp 146—147° (decomp.). *Anal.* Calcd. for $C_{31}H_{52}O_{10}N_4S$: C, 52.52; H, 7.96; N, 7.91. Found: C, 52.53; H, 7.76; N, 8.14.

Dehydroleucomycin-A_3 (12)——To a solution of 5 g of **1** in 500 ml of $CHCl_3$ was added 50.5 g of MnO_2 and the mixture was refluxed for 48 hr with stirring. Then MnO_2 was filtered off and the filtrate was extracted with three 50 ml portions of $CHCl_3$. The combined extract was dried over anhyd. Na_2SO_4 and $CHCl_3$ was evaporated under a reduced pressure to obtain 3.7 g of a brown amorphous powder. It was chromatographed over a Kieselgel G to fractionate 1.2 g of a pure oxide, **12**, which was crystallized from AcOEt; Yield 20%. $[\alpha]_D^{25}$ −39.0° (c=1, l=1, EtOH); UV λ_{max}^{MeOH} mμ (ε) 279 (23,000); IR ν_{max}^{KBr} cm^{-1}: 3400, 2930, 2710, 1723, 1672, 1630, 1590, 1448, 1368, 1293, 1230, 1163, 1075, 1015, 977, 838.

Tetrahydro-dehydroleucomycin-A_3 (13)——A solution of 4.7 g of the dehydro compound (**12**) in 50 ml of EtOH was catalytically hydrogenated in the presence of 500 mg of 5% Pd–C. A theoretical amount of H_2 was taken up in 7 hr and the filtrate was evaporated under a reduced pressure to give 4.54 g (96%) of tetrahydride (**13**). IR ν_{max}^{KBr} cm^{-1}: 3450, 2940, 1730, 1520, 1450, 1370, 1230, 1160, 1060.

7-Hydroxyoctanoic Acid (14)——To a solution of 4.6 g of the tetrahydro compound (**13**) in 50 ml of $CHCl_3$ were added 20.7 ml (1.16M) of a solution of perbenzoic acid (about 4 eq.) in chloroform and 690 mg of *p*-toluenesulfonic acid in 10 ml of $CHCl_3$, and the mixture was allowed to stand for 34 hr in a dark place. The progress of the reaction was checked by the addition of acid solution of KI to the reaction mixture, and perbenzoic acid in the reaction mixture was calculated from titration of the isolated I_2 with $Na_2S_2O_2$ solution. The progress of the reaction was also confirmed by thin-layer chromatography ($CHCl_3$:MeOH:AcOH:H_2O =79:11:8:2). Ether was added to the mixture after completion of the reaction, the solution was extracted with $NaHCO_3$ solution, and then washed with water. The $CHCl_3$ layer was dried over anhyd. Na_2SO_4 and removal of the solvent gave 4.52 g of the oxide. To a solution of 4.52 g of the oxide so obtained in 100 ml of MeOH was added 70 ml of 2N KOH. After standing for 48 hr at room temperature, MeOH was evaporated under a reduced pressure and the residue was extracted with ether to remove a neutral portion. The aqueous layer was acidified with 1N H_2SO_4, then extracted with ether and AcOEt separately. The extract was dried over anhyd. Na_2SO_4 and the combined solvent was evaporated under a reduced pressure to give an oily substance, **14**, which was methylated with CH_2N_2. The methyl ester of **14** was identified with methyl 7-hydroxyoctanoate obtained by synthesis, in retention time on gas liquid chromatography. *Anal.* Calcd. for $C_{19}H_{18}O_3$: C, 62.12; H, 10.40. Found: C, 62.04; H, 10.41. Gas liquid chromatography: PEG 6000, 3 mm×2.6 mm, column temp., 180°, det. temp., 210°, injector temp., 190°, H_2: 60 ml/min; retention time, 13.8 min.

2′-O-Monoacetylleucomycin-A_3 (15)——Ac_2O was added to a solution of 1 g of **1** in 4 ml of acetone and the mixture was allowed to stand for 2 hr at room temperature. The reaction mixture was poured into ice–water, the mixture was adjusted to pH 8.0 with NH_3 water, and extract was dried over anhyd. Na_2SO_4 and evaporation of the solvent left 410 mg of **15** as a white powder. It was crystallized from benzene to 300 mg of **15**, mp 132—135°; $[\alpha]_D^{25}$ −71.6° (c=5, l=1, MeOH), UV λ_{max}^{MeOH} mμ ($E_{1cm}^{1\%}$) 231 (552).

2′-O-Monoacetyl-tetrahydroleucomycin-A_3 (16)——A solution of 500 mg of the monoacetyl compound (**15**) in 10 ml of EtOH was catalytically hydrogenated in the presence of 50 mg of PtO_2 and the same procedure as above gave 440 mg of **16** as a white powder. Yield, 88%. $[\alpha]_D^{25}$ −93.6° (c=5, l=1, MeOH). $[M]_D^{25}$ −818°. *Anal.*. Calcd. for $C_{44}H_{75}O_{10}N$: C, 60.48; H, 8.59; N, 1.60. Found: C, 59.24; H, 8.99; N, 1.70.

9-(3,5-Dinitrobenzoyl)-tetrahydro-2′-O-monoacetylleucomycin-A_3 (17)——To a solution of 500 mg of **16** and 400 mg of 3,5-dinitrobenzoyl chloride in 3 ml of benzene was added 3 ml of pyridine, and the solution was allowed to stand for 2 hr at room temperature. Ether was added to this reaction mixture and the precipitate produced was dissolved by addition of a satud. $NaHCO_3$ solution with stirring. Ether layer was then washed with water, dried over anhyd. Na_2SO_4, and evaporated under a reduced pressure . In order to remove the remaining pyridine, the residue was chromatographed over Silicagel G and 388 mg of **17** was obtained as a white powder. Yield, 54.7%. $[\alpha]_D^{25}$ −87.5° (c=2.4, l=1, MeOH). $[M]_D^{25}$ −934.5°. *Anal.* Calcd. for $C_{51}H_{77}O_{21}N_3$: C, 5.73; H, 7.27; N, 3.94. Found: C, 57.85; H, 7.69; N, 3.47.

9-(3,5-Dinitrobenzoyl)-2′-O-monoacetylleucomycin-A_3 (18)——To a solution of 300 mg of **15** and 230 mg of 3,5-dinitrobenzoyl chloride in 2 ml of benzene was added 2 ml of pyridine and the mixture was allowed to stand for 2 hr at room temperature. After the same procedure as described for **17**, 180 mg of a yellowish powder was obtained. It was chromatographed over Silicagel G to obtain 150 mg (50%) of **18** as an amorphous powder. $[\alpha]_D^{25}$ −113.25° (c=2.4, l=1, MeOH). UV λ_{max}^{MeOH} mμ ($E_{1cm}^{1\%}$) 232 (532).