SYNTHESES OF 5″-DEOXYLIVIDOMYCIN A AND ITS AMINO DERIVATIVE

Sir:

Recently, we have reported[1,2] that an enzymatically inactivated product of lividomycin A by *Escherichia coli* K-12 ML 1410 R-81 carrying R factor or *Pseudomonas aeruginosa* TI-13 is lividomycin A 5″-phosphate. In the present communication, the syntheses of 5″-deoxylividomycin A (II) and 5″-amino-5″-deoxylividomycin A (III) from lividomycin A[3] (I) are reported.

The penta-N-benzyloxycarbonyl-4′, 6′ : 2‴″,3‴″ : 4‴″,6‴″-tri-O-isopropylidene lividomycin A (IV) was prepared from I by the method described in the previous paper[2]. Preferential tosylation of the primary hydroxyl group in ribose moiety of IV with *p*-toluenesulfonyl chloride in dry pyridine at −15°C for 6 hours followed by purification on silicic acid chromatography afforded the 5″-tosylate (V) in a 22% yield, m.p. 133~135° C (dec.). Anal. calcd. for $C_{85}H_{103}N_5O_{30}S$: C 59.81, H 6.08, N 4.10, S 1.88. Found: C 59.71, H 6.24, N 4.27, S 1.93.

Halogenation of V with sodium iodide in dimethylformamide at 80°C for 43 hours in a sealed tube followed by chloroform extraction gave the crude 5″-iodide (VI). The O-isopropylidene groups of VI were removed by hydrolysis with 90% trifluoroacetic acid for 15 minutes at room temperature. The catalytic hydrogenation of the compound (penta-N-benzyloxycarbonyl-5″-deoxy-5″-iodolividomycin A) with 10% palladium-carbon in 45% trifluoroacetic acid under atmospheric pressure followed by column chromatography of Amberlite CG-50 (NH_4^+) afforded II in a 32% yield from V. It shows no definite melting point and darkens at about 190°C. Anal. calcd. for $C_{29}H_{54}N_5O_{17}\cdot 3H_2O$: C 43.60, H 7.57, N 8.77. Found: C 43.65, H 7.62, N 8.71.

For the synthesis of III, the treatment of V with sodium azide in dimethylformamide at 80°C for 18 hours in a sealed tube followed by chloroform extraction gave the crude 5″-azide (VII). By the similar procedures described above, hydrolysis of VII with 90% trifluoroacetic acid followed by catalytic hydrogenation with palladium-carbon afforded III in a 43% yield from V. It shows no definite melting point and darkens at

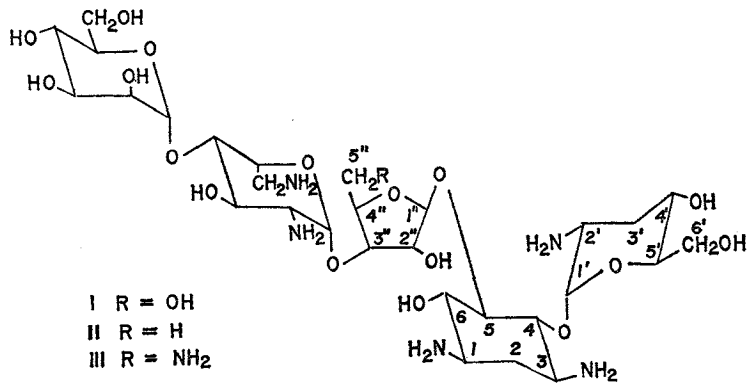

Table 1. The antimicrobial spectra of lividomycin A and its derivatives (mcg/ml)

Test organisms	Lividomycin A (I)	5″-Deoxylividomycin A (II)	5″-Amino-5″-deoxylividomycin A (III)
Staphylococcus aureus FDA 209P	1.56	25	12.5
Staphylococcus aureus Smith	<0.39	0.78	<0.39
Sarcina lutea PCI 1001	6.25	25	100
Bacillus subtilis NRRL B-558	<0.39	6.25	0.78
Escherichia coli NIHJ	3.12	100	50
Escherichia coli K-12	3.12	100	25
Escherichia coli K-12 ML1629	>400	100	200
Escherichia coli K-12 ML1410	3.12	100	100
Escherichia coli K-12 ML1410 R-81	>400	200	100
Shigella sonnei 191-66	12.5	200	100
Salmonella typhosa T-63	1.56	12.5	6.25
Klebsiella pneumoniae PCI 602	3.12	50	25
Proteus vulgaris OX 19	3.12	25	12.5
Pseudomonas aeruginosa A3	12.5	>200	100
Pseudomonas aeruginosa No. 12	50	>200	>200
Pseudomonas aeruginosa 99	200	>200	>200
Pseudomonas aeruginosa TI-13	50	200	100

about 170°C. Anal. calcd. for $C_{29}H_{56}N_6O_{17}\cdot 2H_2O$: C 43.71, H 7.59, N 10.55. Found: C 43.40, H 7.63, N 9.95.

The antimicrobial spectra of I, II and III are shown in Table 1, showing that II and III have generally weaker activity against various test organisms than I, but it is noteworthy that II and III are more active than I against lividomycin-resistant *Escherichia coli* K-12 ML1629 and K-12 ML1410 R-81 carrying R factor.

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References

1) KONDO, S.; H. YAMAMOTO, H. NAGANAWA, H. UMEZAWA & S. MITSUHASHI: Isolation and characterization of lividomycin A inactivated by *Pseudomonas* and *Escherichia coli* carrying R factor. J. Antibiotics 25: 483~484, 1972
2) YAMAMOTO, H.; S. KONDO, K. MAEDA & H. UMEZAWA: Synthesis of lividomycin A 5''-phosphate, an enzymatically inactivated lividomycin A. J. Antibiotics 25: 485~486, 1972
3) ODA, T.; T. MORI, Y. KYOTANI & M. NAKAYAMA: Studies on new antibiotic lividomycins. IV. Structure of lividomycin A. J. Antibiotics 24: 511~518, 1971