SYNTHESIS OF LIVIDOMYCIN A 5''-PHOSPHATE, AN ENZYMATICALLY INACTIVATED LIVIDOMYCIN A

Sir:

As described in the preceding paper[1], lividomycin A[2] (I) is phosphorylated to its 5''-phosphate by ATP and an enzyme prepared from *Escherichia coli* K-12 ML1410 R-81 carrying R factor and *Pseudomonas aeruginosa* TI-13. This structure of the phosphorylated and inactivated lividomycin A was proposed from chemical evidence and pmr data. In this communication, the synthesis of lividomycin A 5''-phosphate is reported.

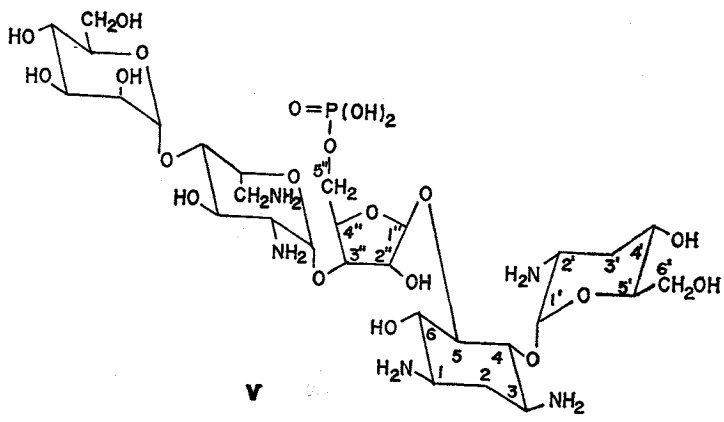
The penta-N-benzyloxycarbonyllividomycin A (II) was prepared from I by the usual SCHOTTEN-BAUMANN procedure in a 95 % yield, m.p. 135~150°C (dec). Found: C 57.68, H 6.18, N 4.92, O 30.44. Anal. calcd. for $C_{69}H_{85}N_5O_{28}$: C 57.85, H 5.98, N 4.88, O 31.27.

Acetonation of II with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid in dimethylformamide at 110°C for 4 hours afforded the tri-*O*-isopropylidene derivative (III) in a 49 % yield, m.p. 129~133°C (dec). Found: C 60.44, H 6.39, N 4.80, O 28.66. Anal. calcd. for $C_{78}H_{97}N_5O_{28}$: C 60.33, H 6.29, N 4.51, O 28.85.

Preferential phosphorylation[3,4] of the sole primary hydroxyl group in ribose moiety of III with diphenyl phosphorochloridate in dry pyridine gave penta-*N*-benzyloxycarbonyl-4',6':2'''',3'''':4'''',6''''-tri-*O*-isopropylidene lividomycin A 5''-diphenylphosphate (IV) in a 55 % yield, m.p. 125~130°C. Found: C 60.57, H 6.07, N 3.70, O 27.69, P 2.46. Anal. calcd. for $C_{90}H_{106}N_5O_{31}P$: C 60.56, H 5.99, N 3.92, O 27.79, P 1.74.

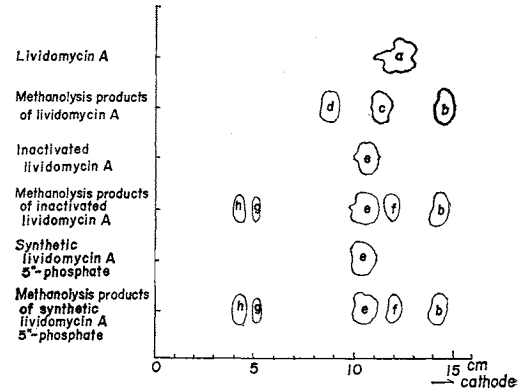
The protective groups of IV were stepwise removed by catalytic hydrogenolysis with palladium black in acetic acid under atmospheric pressure, hydrolysis with 90 % trifluoroacetic acid followed by hydrogenolysis with platinum oxide in 50 % aqueous ethanol in a PARR apparatus at 4.3 atmosphere (starting pressure) to afford synthetic lividomycin A 5''-phosphate (V). The product was purified by a column of Amberlite CG-50 (NH_4^+). It does not melt up to 210°C, $[\alpha]_D^{20}$ +54.4° (*c* 1.47, H_2O). Found: C 37.58, H 7.35, N 7.84, P 3.36. Anal. calcd. for $C_{29}H_{56}N_5O_{21}P \cdot 5H_2O$: C 37.38, H 7.14, N 7.52, P 3.32.

V was confirmed to be identical with the inactivated lividomycin A[1] in all respects including the pmr



V

Fig. 1. High-voltage paper electrophoresis of methanolysis products of lividomycin A, inactivated lividomycin A and synthetic lividomycin A 5''-phosphate.



		Ninhydrin	HANES reagent
a	Lividomycin A	+	−
b	3'-Deoxyparomamine	+	−
c	Methyl lividobiosaminide	+	−
d	Methyl lividotriosaminide	+	−
e	Inactivated livldomycin A or lividomycin A 5''-phosphate	+	+
f	Lividomycin B 5''-phosphate	+	+
g	Methyl lividobiosaminide phosphate	+	+
h	Methyl lividotriosaminide phosphate	+	+

spectrum. On high-voltage paper electrophoresis using formic acid-acetic acid-water (25 : 75 : 900 in volume) at 3,000 volts for 20 minutes, the methanolysis products of **V** (refluxed in 0.4 N hydrogen chloride in methanol for 6 hours) and the inactivated lividomycin A were compared as shown in Fig. 1.

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