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

Sir:
As described in the preceding paper,1) lividomycin A (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_{5}O_{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_{5}O_{28}: C 60.33, H 6.29, N 4.51, O 28.85.

Preferential phosphorylation 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_{5}O_{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^\circ +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_{48}N_{5}O_{25}P.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 in all respects including the pmr
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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