A NOVEL FATTY ACID FROM LASPARTOMYCIN

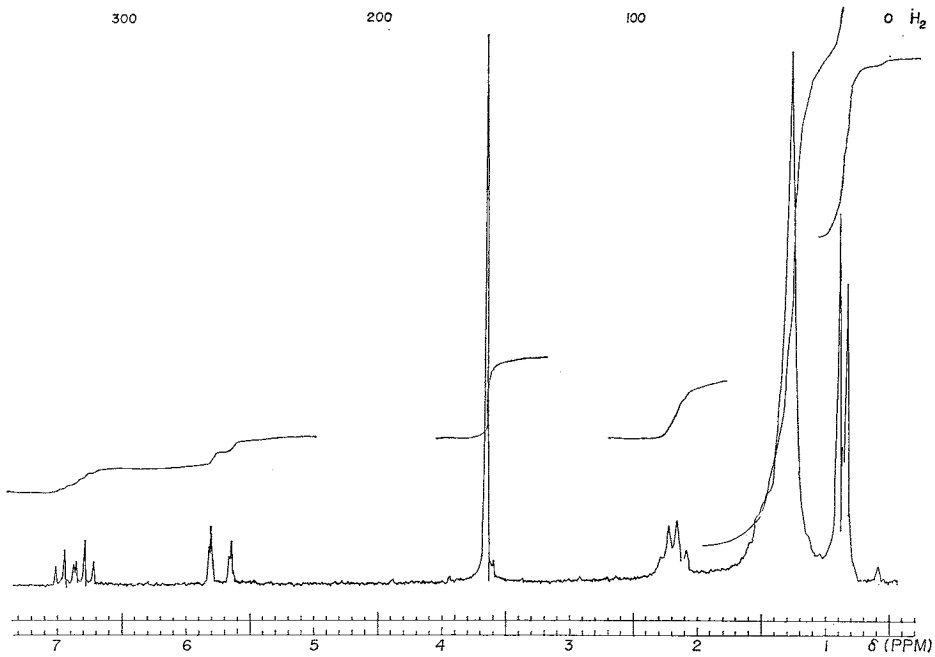
Sir:

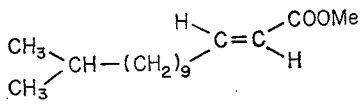
Laspartomycin[1] is a peptide antibiotic inhibiting Gram-positive bacteria. It is a member of the group of antibiotics to which amphomycin, zaomycin, crystallomycin, aspartocin, glumamycin and tsushimycin belong. All these antibiotics are peptides which are acylated by fatty acids. In the present communication the structure of the fatty acid moiety of laspartomycin is described.

Laspartomycin was hydrolyzed with 6 N hydrochloric acid for 20 hours at 105°C in a sealed tube. The hydrolysate was extracted with diethyl ether and the ethereal solution was then treated with diazomethane. The residue present in the solution was examined by gas-liquid chromatograpy using a polyester column. A mixture of methyl ester of fatty acids was seen in which there were one major (70.5 %), three minor (12.6, 8.7 and 4.6 %) and other trace components.

The major component (I) present in the mixture of methylated fatty acids was isolated by silica-gel column chromatography and preparative gas-liquid chromatography. It has the molecular formula $C_{16}H_{30}O_2$ (M. W. 254) as indicated by elemental analysis (Calcd: C 75.53, H 11.89, O 12.58. Found: C 75.38, H 12.46, O 12.53.) The high-resolution mass spectrum showed a molecular ion with m/e 254.226 (Calcd. 254.225). The n.m.r. spectrum of I in carbon tetrachloride solution measured at 100 MHz is shown as Fig. 1. There are a six-proton doublet at δ 0.88 (splitting 6.3 Hz), a seventeen proton multiplet at δ 1.0~1.7, a two-proton multiplet at δ 2.20, a three-proton singlet at δ 3.66, a one-proton doublet of triplets at δ 5.72 (splittings of 15.5 and 1.5 Hz) and a one-proton doublet of triplets at δ 6.86 (splittings of 15.5 and 7.0 Hz). The UV absorption of I at 210 mμ (ε 12,600) in methanol solution, the strong IR absorption at 975 cm^{-1} and the large coupling constant (15.5 Hz) of the olefinic protons in the n.m.r. spectrum all suggest the presence of a *trans*-α, β-unsaturated carboxylic acid ester system. The existence of isopropyl moiety in I was suggested by the presence in the n.m.r. spectrum of a doublet signal of six protons at δ 0.88 which collapsed to a singlet on irradia-

Fig. 1. The n.m.r. spectrum of *trans*-2-isopentadecenoic acid methyl ester (I) (100 MHz, CCl_4)





(I)

tion at δ 1.51. From all these observations it was assumed that the major fatty acid ester (I) recovered from laspartomycin is *trans*-2-isopentadecenoic acid methyl ester.

This structural assignment was confirmed by the following experiments. On catalytic hydrogenation (PtO_2 in MeOH) compound I gave a dihydro-derivative (II), the molecular formula of which was determined by mass spectrometry ($C_{16}H_{32}O_2$: m/e 256). Also, the mass spctrum and the n.m.r. spectrum of II were consistent with it being isopentadecanoic acid methyl ester. Oxidative degradation of I using the periodate-permanganate method gave a fatty acid having two fewer carbon atoms as indicated by mass spectroscopic examination of the methyl ester ($C_{14}H_{28}O_2$: m/e 228). This result supports the assignment of the double bond in I to the 2, 3 position.

From the results described in this communication the major fatty acid residue present in laspartomycin is *trans*-2-isopentadecenoic acid. The structures of the fatty acids known to be present in antibiotics related to laspartomycin are : *cis*-3-iso- and *cis*-3-anteisopentadecenoic acids in aspartocin[2] ; 3-iso-tridecenoic acid in glumamycin[3] ; *cis*-3-anteisopentadecenoic acid and *cis*-3-isotetradecenoic acid in tsushimycin[4] ; and *cis*-3-anteisotridecenoic acid in amphomycin[4]. All of these previously identified acids are *cis*-β,γ-unsaturated. Information is not available concerning the configuration of the 3-isotridecenoic acid of glumamycin. However, it is most interesting to note that the fatty acid present in laspartomycin is *trans*-α,β-unsaturated in apparent contrast to the acids typical of the related group of antibiotics.

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