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THE STRUCTURE OF CEPHALONIC ACID, A PENTAPRENYL TERPENOID[1)]

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Cephalosporium caerulens is known as a helvolic acid-producing microorganism[2)] and has recently been found to produce a new compound which shows weak activity against Staphylococcus aureus. We report herein the isolation and the structure elucidation of this metabolite, which is named cephalonic acid. Extraction of the cultured broth (6 L, 6 days) with ethyl acetate at pH 3 and fractionation of the extract by silica gel chromatography afforded 0.023g of cephalonic acid, in addition to 1.42g of helvolic acid, 0.293g of ergosterol, etc.. Although one fermentation accidentally gave rise to a comparatively large amount of this compound, this could not be repeated thereafter. Cephalonic acid m.p. 139°; $C_{25}H_{36}O_4$; mol. wt. 400; $(\alpha)_D$+76.2 (c=0.54, $CHCl_3$), shows UV absorption maximum at 259 mμ (ε, 11,700) and IR absorption bands at 3000, 1680, 1610 cm^{-1}.

Bromoacetylation of methyl cephalonate with bromoacetyl bromide in benzene afforded the bromoacetate, m.p. 102°; $C_{28}H_{39}O_5Br$. The molecular structure and the absolute configuration of the bromoacetate have been determined by three-dimensional X-ray crystallographic analysis. The crystals from methanol solution are orthorhombic with the lattice constants a=11.36Å, b=29.41Å and c=8.13Å. The spece group was found to be $P2_12_12_1$ and four molecules are contained in a cell. X-ray intensity data were collected by equi-inclination Weissenberg photographs using Cu-Kα radiation and were estimated visually (total of 1791 non-zero reflections). The structure was solved by the heavy atom method. Since the bromine atom (x=0.218, y=0.1115 and z=0.250 obtained

from a Patterson-Harker section) was in a unfortunate position, the electron density map calculated from the bromine atom was difficult to interpret due to excess symmetry. Taking into account a five-membered ring which was rather distinctly discriminable several successive Fourier and difference Fourier syntheses yielded the whole structure. The first two cycles of a full-matrix least-squares refinement gave an R value of 0.166[3]. Fig. 1 shows the perspective drawing of the structure of methyl cephalonate bromoacetate including the absolute configuration which was determined by the anomalous dispersion effect of the bromine atom.

The results revealed that the structure of cephalonic acid is expressed by I. The C_{15} position of the side chain possesses an opposite configuration to the corresponding position of the sterol side chain. The structure I is consistent with chemical informations, which will be reported in a subsequent paper.

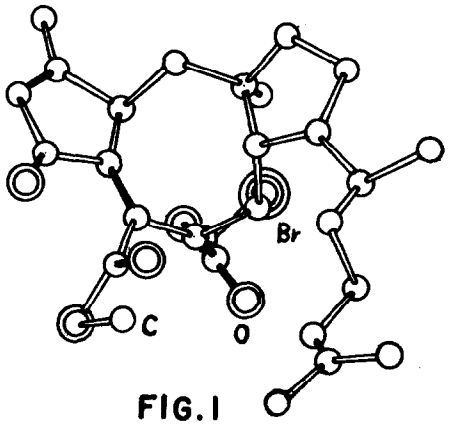
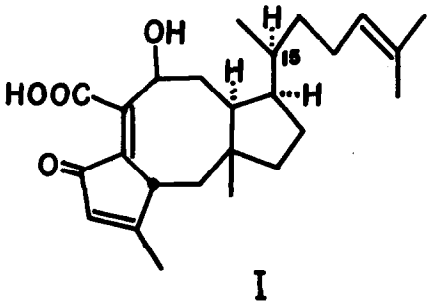


FIG.1



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3. The full account of the analysis will be published elsewhere.