Communication to the editors

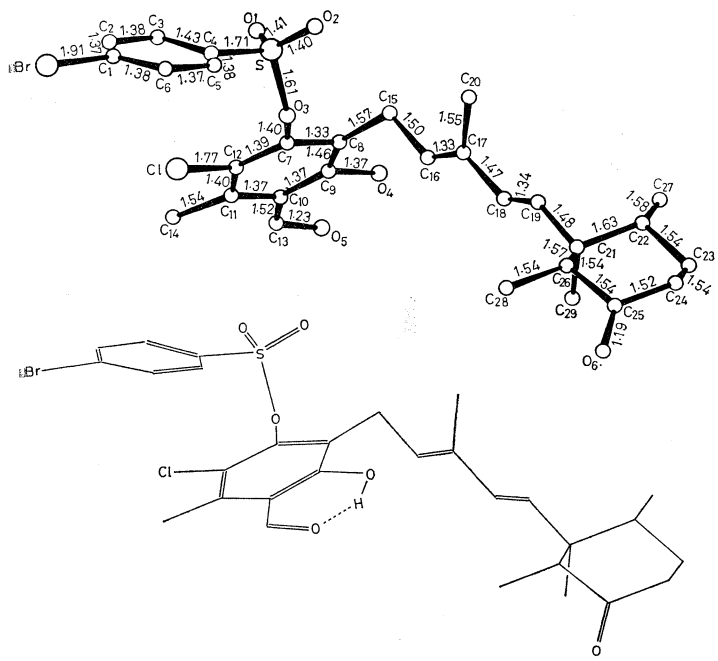
THE MOLECULAR STRUCTURE OF ASCOCHLORIN

Sir:

Ascochlorin was isolated by TAMURA *et al.*[1] from the filter cake of the fermented broth of *Ascochyta viciae* LIBERT. The antibiotic shows inhibitory activities against some viruses and fungi *in vitro*. In this communication we wish to report the structure of ascochlorin.

The *p*-bromobenzenesulfonyl derivative of ascochlorin was subjected to X-ray structure analysis. The crystal belongs to orthorhombic system. From precession photographs, lattice constants were determined to be a=13.86, b=30.04 and c=6.82 Å. Systematic absences of reflections on the photographs indicated the space group of this crystal to be D_2^4-$P2_12_12_1$. Diffraction data were collected from the multiple film WEISSENBERG photographs taken with CuKα radiation. The total number of independent reflections was 1627. Intensities were measured visually by comparing with a standard intensity scale. For the structure determination the heavy atom method was applied; at first the structure factors were calculated (R=43.8 %) with the positional parameters of bromine atom which were determined from the three-dimensional Patterson function. On the first FOURIER map, distinct peaks of the chlorine atom and *p*-bromobenzenesulfonyl group were found and the gross features of the ascochlorin molecule were revealed. Several repeated cycles of structure factor and FOURIER calculations enabled us to determine the positions of all atoms except hydrogen. The R factor at this stage was 24.4 %. The refinement was carried out by the method of least squares using block-matrix approximations. The anisotropic thermal motions were taken into account only for the bromine atom. From the results of the third cycle of this calculation the locations of the oxygen atoms of the ascochlorin molecule were clearly found; namely thermal parameters were smaller than the others and the bond distances suggested the existence of keto, aldehyde and hydroxyl groups. Finally, the least-squares refinements were carried out with the anisotropic thermal parameters for all atoms (38 atoms). The final R factor was 10.2 % and the average value of the standard deviations of the atomic distances was 0.027 Å. In Fig. 1, the absolute configuration of ascochlorin *p*-bromobenzenesulfonate is shown as determined by BIJVOET's method using the anomalous dispersion of CuKα radiation by bromine, chlorine and sulfur atoms. The ascochlorin molecule consists of phenyl and cyclohexanone moieties connected to each other through a zigzag methyl pentadiene chain. The phenyl moiety is a derivative of salicylaldehyde, and hydroxyl, chlorine and methyl groups are attached at C_7, C_{12}, and C_{11} carbon atoms of

Fig. 1. Absolute configuration of ascochlorin *p*-bromobenzenesulfonate.



the benzene ring. As is expected, the atoms of salicylaldehyde lie in a plane; deviations from the plane do not exceed 0.07 Å. This fact and oxygen-oxygen distance between the aldehyde and hydroxyl groups (2.57 Å) suggest the existence of an intramolecular hydrogen bond. The cyclohexanone ring adopts a typical chair form; two carbon atoms of C_{25} and C_{22} deviate +0.64 and −0.70 Å, respectively, from the plane formed by the four carbon atoms of C_{21}, C_{23}, C_{24} and C_{26}. Three methyl groups are attached to the ring; two of them are in the equatorial position (C_{27}, C_{28}) and the other is in the axial (C_{29}). The pentadiene chain has two double bonds at C_{16}~C_{17} and C_{18}~C_{19} with all-*trans* configuration. The internal rotation angle of the two double bonds around the C_{17}~C_{18} bond is 175.9°.

The structure presented here is completely consisted with the spectral evidence reported previously[1]. The nmr spectrum ($CDCl_3$) showed five methyl signals at τ 9.31 (singlet), 9.23 (doublet), 9.16 (doublet), 8.76 (singlet) and 8.10 (singlet); olefinic protons at τ 4.06 and 4.67 (1H, respectively) coupled with 16 cps, indicating trans configuration; olefinic proton (triplet, 1H) at τ 4.50. A signal at τ −0.68 (1H) clearly indicates the presence of aldehyde group and a signal at τ −2.68 (1H) is of a proton of phenolic hydroxyl which forms a intramolecular hydrogen bond with the aldehyde. The mass spectrum of ascochlorin showed an abundant peak at m/e 199 accompanied with a characteristic peak at 201 indicating the presence of chlorine atom in the ion. This peak corresponds to a tropylium ion formed by fission between C_{15} and C_{16}.

Therefore, ascochlorin represents a new antibiotic structure. The details of this study will be presented elsewhere.

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Reference

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