THE CRYSTAL AND MOLECULAR STRUCTURE OF BOSTRYCIN p-BROMOBENZOATE, A DERIVATIVE OF BOSTRYCIN

Akio Takenaka, Akio Furusaki and Tokunosuké Watanabé

Faculty of Science, Kwansei Gakuin University,

Nishinomiya, Japan

and

Toshiharu Noda, Teruo Take, Tetsuo Watanabe and Jin-nosuke Abe

Research Institute, Toyo Jozo Co., Ltd.,

Ohito, Tagata, Shizuoka, Japan

As described in the preceding paper, bostrycin, an antibiotic produced by *Bostryconema alpestre*, was isolated recently with chloroform extraction from the cultured broth of this parasitical mould on *Polygonum filiforme* Thunb. var. *neofiliforme* Ohwi. This antibiotic is active mainly against some species of Gram-positive bacteria. In order to find out the molecular structure of bostrycin and establish its stereochemistry including the absolute configuration, we have studied the crystal structure of one of *p*-bromobenzoate derivatives, ($C_{23}H_{19}O_7Br$), hereafter XIa, by the X-ray method, parallel with an chemical investigation[1]. This paper will describe the outline of the structure determination of XIa.

Large single crystals of XIa were grown from dimethyl formamide solutions. Crystals, suitable for the structure determination, were ground to a cylindrical form with the solvent. The crystal is found to be monoclinic with the space group $P2_1$ and the unit-cell dimensions, $a = 13.294 \pm 0.003$, $b = 26.495 \pm 0.003$, $c = 7.225 \pm 0.002$ Å and $\beta = 90.63 \pm 0.01°$. In order to explain the chemical composition of the crystal, $C_{26}H_{26}O_8NBr$, given by an elementary analysis and the observed density, 1.478 g·cm^{-3}, the unit cell should contain in addition to four

molecules of XIa four molecules of dimethyl formamide, hereafter DMF. It follows
that there are each two molecules of XIa and DMF in the asymmetric unit.

For the purpose of collecting intensity data, equi-inclination integrating
Weissenberg photographs were taken with nickel-filtered Cu $K\alpha$ radiation around
the a- and c-axes. Intensities of the diffraction spots were measured visually
by comparison with a standard intensity scale using the multiple-film technique.
These intensities were corrected for the Lorentz and polarization factors in the
usual way. Relative values of the observed structure factors of 4819 reflections
were placed on an absolute scale by Wilson's method.

The positions of the two Br atoms in the asymmetric unit were derived from
a three-dimensional sharpened Patterson function. A three-dimensional electron-
density distribution was computed with all the observed structure factors using
phases based on the two Br atoms alone. Reasonable atomic positions of the two
independent molecules of XIa could be found out in the arrangement of significant
peaks appearing in the Fourier map, but it was difficult to assign ten peaks to
atoms of the two molecules of DMF. Using the coordinates of the sixty-two
independent atoms thus obtained, the second Fourier synthesis was carried out.
The resulting electron-density map showed that the positions of all the sixty-two
atoms mentioned above were essentially correct, and also revealed the atomic
positions of the two remaining molecules of DMF.

The atomic coordinates and isotropic temperature factors of all the seventy-
two independent atoms were refined by the diagonal-matrix least-squares method
using all the 4819 data. After two cycles of the refinement, the structure was
further confirmed by a difference synthesis. Two more cycles of the block-
diagonal-matrix least-squares refinement assuming anisotropic thermal motions for
the two Br atoms were carried out using 3373 data, omitting very weak reflections.
At the present stage, the discrepancy index R is 0.138 and the average standard
deviations in positional parameters are about 0.003 for Br, 0.02 for O, 0.03 for
N and 0.03 Å for C atoms. The absolute configuration of XIa was also determined
from the Bijvoet relations using the dispersion of Cu $K\alpha$ by the Br atoms.

The structural formula thus obtained is shown in Fig.1, including the
absolute configuration. Aside from the absolute configuration, this result

coincides with the formula deduced by T. Noda *et al.*[1] from their chemical investigation. Bond lengths and angles of both each the two independent molecules of XIa and DMF evaluated from the atomic coordinates are all reasonable.
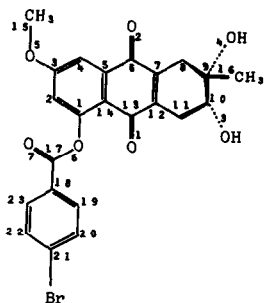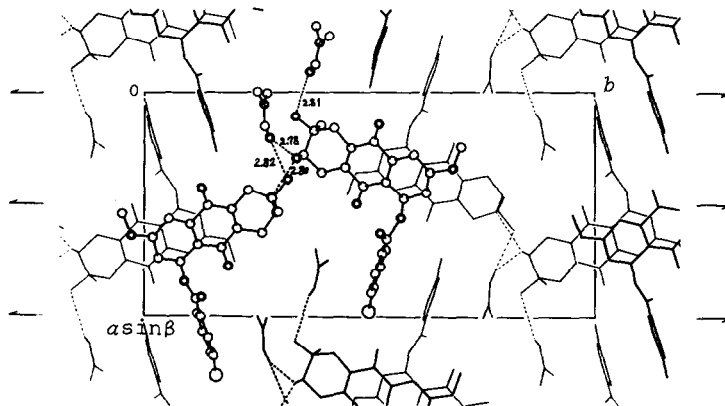

Fig.1.

Fig.2. The crystal structure of bostrycin
p-bromobenzoate viewed down along the *c*-axis.

The molecule characterized by a naphthoquinone part contains, in addition to a cyclohexene ring fused at C(7) and C(12) with the quinone part, five substituent groups (a methyl, a methoxyl, two hydroxyl and a *p*-bromobenzoate groups). The two independently determined molecules have the same stereo-structure except the benzoate groups. The naphthoquinone parts and the methoxyl groups at C(3) are nearly on the same plane. The cyclohexene rings having a double bond are of the half-chair form. Around the C(9)-C(10) bond, the methyl group C(16) and hydroxyl group O(3), both axial, keep almost the *trans* conformation, and the two hydroxyl groups, O(3) and O(4) the latter being equatorial, the *gauche*. The benzoate groups are approximately of the planar structure. The two molecules have, however, different conformations which arise from the twisting of the benzoate group around the C(1)-O(6) bond. In one of the two molecules, O(7) of the carboxyl group is on the same side as the methyl group C(16) from the naphthoquinone plane, while, in the other, O(7) is on the opposite side of C(16). A remarkable feature of the molecular conformation is that the interatomic distances C(17)···O(1) are 2.71 Å in one of the molecules and 2.86 Å

in the other, both of which are considerably shorter than the sum of the van der Waals radii of the two atoms. This suggests an additional attractive force acting between these two atoms. The twisting of the bond C(1)-O(6) may arise from the balance of the attraction between O(1) and C(17) and the repulsion between O(1) and O(7), which gives two equilibrium positions for O(7). The two conformers have almost the relation of mirror-image with each other with respect to the naphthoquinone plane, except for the dissymmetric aliphatic carbon atoms, C(9) and C(10). Since the dissymmetric aliphatic part lies far from the benzoate group, the interactions between them may be too weak to break the mirror-image relation of the two conformers.

As shown in Fig.2, the independent two molecules of XIa and two molecules of DMF are linked together by four hydrogen bonds (2.80, 2.78, 2.82 and 2.81 Å) among the four hydroxyl groups of the XIa molecules and the two carbonyl groups of the DMF molecules. One of the four is formed between the hydroxyl groups of the two XIa molecules. The two DMF molecules taking the planar structure lie in the cavities arising from the packing of the bulky XIa molecules, to which they are linked by the remaining hydrogen bonds; one of the two accepts two hydrogen atoms from the two XIa molecules and the other a hydrogen atom from one of the two. Thus these four molecules can be taken as forming an associated molecule. Between these associated molecules, intermolecular atomic approaches are mainly the van der Waals contacts.

The detailed informations of the present structure will be described in a full paper to be published in the near future.

REFERENCE

(1) T. Noda, T. Take, M. Otani, K. Miyauchi, T. Watanabe and J. Abe, *Tetrahedron Letters*, the preceding paper.