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THE X-RAY STUDY OF ACETYL-BROMOACETYLDIHYDROENMEIN

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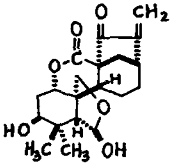
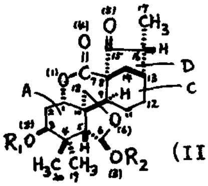
Enmein, $C_{20}H_{26}O_6$, is a diterpene bitter principle isolated from Isodon trichocarpus Kudo and its structural study has been carried out chemically by several research groups for years (1, 2,3,4,5). Parallel to the chemical investigations of enmein, we have performed the X-ray study of its heavy atom derivative and elucidated the constitution and stereochemistry of enmein as (I), apart from the absolute configuration.


(I)



(II)

The sample suitable for the X-ray analysis, acetyl-bromoacetyldihydroenmein, $C_{24}H_{31}O_8Br$, m.p. 233-235° (II; R_1=Ac, R_2= $BrCH_2CO$) was prepared from monoacetyldihydroenmein (1) (II; R_1=Ac, R_2=H) and obtained as crystals of *orthorhombic system* with the space group, P $2_12_12_1$ and the cell dimensions,

a=9.78±0.02 Å, b=15.25±0.02 Å, c=16.13±0.02 Å.

It was converted back to dihydroenmein (II; $R_1=R_2=H$) in a good yield, so that no skeletal change was conceivable during the preparation. The crystal density was determined to be 1.464 g./cm^3 by flotation method using a mixture of benzene and carbon tetrachloride, corresponding to the calculated value: 1.456 g./cm^3 with four molecules in the unit cell. Three-dimensional data of $0kl \sim 7kl$, $h0l \sim h1l$ and $hk0 \sim hk10$ were collected from equi-inclination Weissenberg photographs taken with copper Kα radiation and intensities were estimated visually using multiple-film and step-wedge techniques. The usual Lorentz and polarization corrections were applied and the 2958 independent structure factors were finally evaluated.

The positions of the bromine atoms were initially determined by the calculation of the two-dimensional Patterson and sharpened Patterson syntheses along the a, b and c crystal axes. Phase angles calculated from the bromine positions were compared with the observed structure factors and the electron density projections on (100), (010) and (001) were once calculated, resulting the serious overlapping of the atoms; and therefore further study was carried out by the three-dimensional analysis.

The co-ordinates of the bromine atoms were confirmed and refined from the sections through the three-dimensional Patterson and sharpened Patterson functions at x=1/2, y=1/2 and z=1/2. Structure factors were computed, based on these atomic positions and the first three-dimensional Fourier synthesis utilizing the phase angles thus derived afforded the electron density map, which exhibited twelve light atoms (C_6, C_8, C_9, C_{10}, C_{12}, C_{15}, C_{18}, O_3, O_4, O_5, O_6 and O_8) as well-defined peaks. These were included in the next structure factor calculation assuming all were carbon atoms, and eight atoms (C_1, C_4, C_5, C_{11}, C_{16}, C_{17}, O_1 and O_2) were found in the second Fourier map. The third set of calculation in a similar fashion showed up further six atoms (C_2, C_7, C_{14}, C_{19}, C_{20} and C_{23}) and the difference-Fourier calculation based on the structure factors using positions of the above atoms ($R=0.42$) pointed out the last six atoms and differentiated all oxygen atoms from carbon atoms except O_7 of the acetate group, which was later identified from the bond-length calculation. Final Fourier functions were then computed and the superimposed contour sections illustrating the three-dimensional electron density distribution drawn parallel to (100) are shown in FIG. 1 and the crystal structure viewed along the a axis is illustrated in FIG. 2. · For correction of a pronounced anisotropic thermal vibration of the bromine atom in

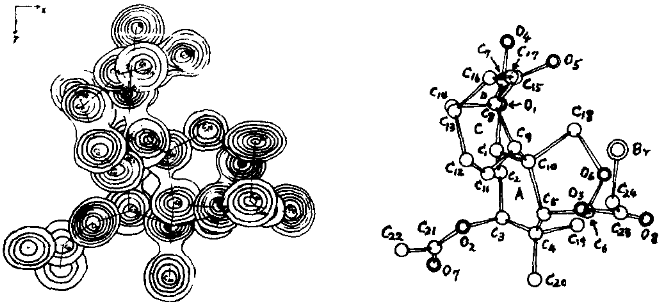


FIG. 1

the c-direction, were placed two bromine atoms of 1/2 weight along the c axis (6) and the R factor at this stage was 0.20. Further refinement was performed by the three-dimensional least squares method including anisotropic temperature factors for each atom[*1] and the R factor was reduced to 0.11_4.

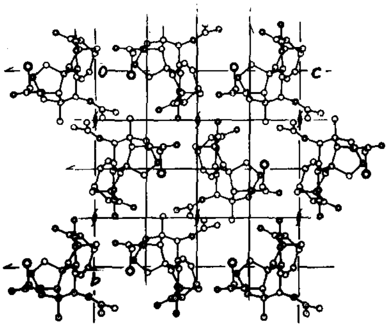


FIG. 2

In the stereochemical structure of acetyl-bromoacetyldihydroenmein, conformation of ring A is of a chair form, whereas ring C have a boat conformation. The juncture between ring A and the five-membered ring having a hemiacetal moiety is in a cis-fusion and the bond C_{10}-C_{18} is axially oriented from ring A. The C_{14} of the [3,1,2]bicycloöctane system is at the opposite side of C_{18} and methyl group C_{17} is in the relation of trans to the bridge carbon atom C_{14}. The O_1 of the six-membered lactone ring is of a equatorial

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[*1] Busing and Levy's program, modified to accomplish the refinement of large structures.

configuration and the acetoxyl group at C_3 is oriented axially in ring A.

The present study revealed that the chemical structure of enmein including its relative configuration is expressed as (I), which coincides the result of the chemical investigations (7).

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