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THE CRYSTAL AND MOLECULAR STRUCTURE OF BROMOHELENALIN*

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The structure of the biogenetically abnormal sesquiterpene lactone tenulin (I), (1-3) the bitter principle of various Helenium species, was deduced from chemical and spectroscopic evidence (4) and confirmed more recently by X-ray analysis (5) of bromoisotenulin (II) which also led to the depicted relative stereochemistry.

Tenulin has been related to several other sesquiterpene lactones, the most important of which is helenalin (6), the main constituent of Helenium autumnale L. and several other Helenium species. A complex series of arguments based on the known multifarious transformations of helenalin, tenulin, and their congeners led to the conclusion that helenalin

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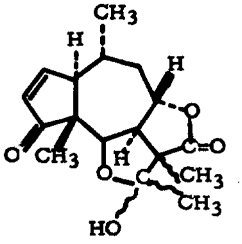
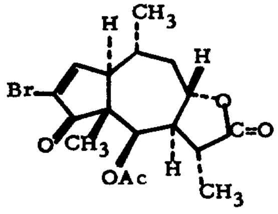
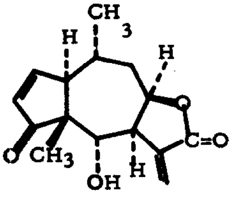
should be represented by III (7). The work described in this communication was undertaken to provide independent proof for the structure of helenalin.



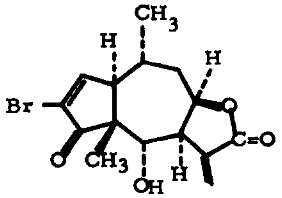
I



II



III



IV

The results confirm the postulated formula and support the validity of the arguments used previously for assignment of stereochemistry.

Treatment of helenalin with bromine in glacial acetic acid furnishes dibromohelenalin which on recrystallization from 50% ethanol-water eliminates hydrogen bromide and forms bromohelenalin (IV).* Single crystals of IV were grown by slow evaporation of the solvent. Precession and Weissenberg photographs were taken using CuK α-radiation. The crystal was orthorhombic with unit cell dimensions a = 8.91 Å, b = 12.28 Å and c = 13.17 Å. The space group (8) was $P\,2_1 2_1 2_1$, since h00, 0k0 and 00ℓ reflections were present only for h, k and ℓ = 2n. The crystal density was measured by the floatation method using a calcium chloride

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* For details of this procedure see R. Adams and W. Herz, J. Am. Chem. Soc. **71**, 2546 (1949). The compound was prepared for us by Dr. P. Jayaraman.

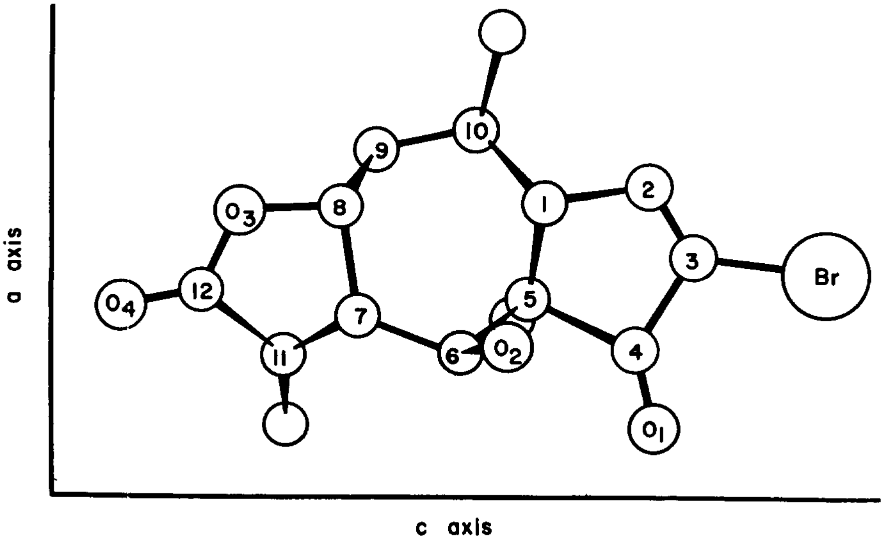
solution. The measured density was 1.553 g. cm^{-3}. On the basis of four molecules per unit cell, the calculated density is 1.573 g. cm^{-3}.

Intensities for five levels (0kℓ through 4kℓ) were recorded with an integrating Weissenberg Camera using the multiple film technique and the equi-inclination method. A total of 1204 non-extinct reflections were measured using a photodensitometer to scan the films. Level to level scaling factors were obtained from precession photographs. Lorentz and polarization corrections were made (no absorption corrections were included) and the intensities were converted to structure amplitudes. These were then rescaled to an approximate absolute scale by a Wilson Plot (9).

The structure analysis was started by calculating the three dimensional Patterson map, the bromine position for the asymmetric unit being determined from the most intense Patterson peaks. A reliability value of R = 0.42 was obtained using only the bromine position. The first three dimensional electron density map gave a slight shift in the X coordinate of the bromine atom and strong peaks for five other atoms. The refinement proceeded normally resulting in a chemically plausible structure. The sixth Fourier map gave the complete molecule. Peaks in the electron density map were sufficiently well resolved to allow positive identification of the four oxygen atoms. Up to this point all atoms except the bromine were considered to be carbons. The resulting R value was 0.227. Two more three dimensional Fourier maps gave further improvement in the atom positions but no change in the structure of the molecule. A least squares refinement was then used to improve the atom positions and assign individual isotropic temperature factors. The final value of the reliability factor for the assumed structure was R = 0.171.

The XZ projection of the molecule* making up the asymmetric unit is shown in Figure 1. The long axis of the molecule lies parallel to the

FIG. 1



Z axis with the cyclopentenone ring in the XZ plane. Therefore, most of the structural features are clearly shown in the projection. The seven membered ring is in a boat form with the 1 and 5 junctions <u>trans</u> and the lactone junction is <u>cis</u>. Thus, the relative stereochemistry is identical with (IV) that derived from the correlation arguments. The conformation of the molecule is somewhat distorted from that predicted by the Dreiding model. This distortion is probably the result of several strong 1-3 interactions.

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* The crystal axis and Cartesian axis designation here are used interchangeably where X = a, Y = b and Z = c.

The bond lengths calculated from the final atomic positions all agree well with accepted values except for C_3-C_4, C_4-C_5 and C_7-C_8 which are within 15% of accepted values. These errors are undoubtedly responsible for the magnitude of R. Further refinement is necessary to obtain better bond lengths and angles and will be carried out at a later date.

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