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THE COMPLETE STRUCTURES OF PULCHELLIDINE AND PULCHELLIN

A CRYSTALLOGRAPHIC STUDY OF 11,13-DIBROMOPULCHELLIN[*]

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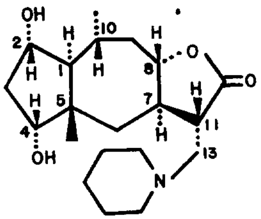
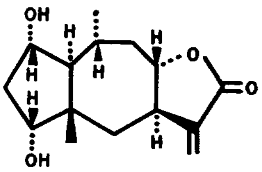
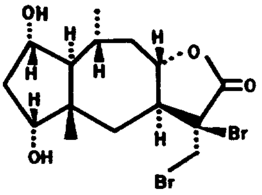
The stereostructures of pulchellidine(I) and pulchellin(II) have been forwarded by chemical and spectral studies in the preceeding communications(1) (2). Certain umbiguity suspended in the ring junctures of I, II and their analogues have, however, precluded a complete structure determination, because of the difficulties encountered in the interpretation of some chemical studies. We decided to confirm this point, i.e. the stereochemistry of C_1- α-H to C_5- β-CH_3 as represented in I and II, and further to establish their absolute configurations by X-ray crystallographic analysis.



I



II



III

As one of the heavy atom containing derivatives of pulchellidine the hydrobromide: $C_{20}H_{33}O_4N\cdot HBr$; mp 208-210°; $\nu^{CHCl_3}_{cm^{-1}}$ 3390(hydroxyl), 2620, 2550 ($\overset{+}{\geq}NH$), 1774(γ-lactone) was prepared, but it proved to be unsuitable like other available quaternarized

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nitrogen derivatives due to its high thermal atenuation and vulnerability to moisture. Halogenoacyl substitutions of the hydroxyl group in pulchellidine failed in our hands probably due to inertness of the group for such bulky reagents and instability of α-piperidinomethyl-γ-lactone moiety. Thus we turned attention to pulchellin(II), the deaminative derivative of I(1). After several unsuccessful attempts to prepare halogenoacyl derivatives of II, the bromination of II in chloroform gave in almost quantitative yield 11,13-dibromopulchellin(III), that formed the first usable crystal for the X-ray analysis: $C_{15}H_{22}O_4Br_2$: mp 113 - 115°; $\nu_{cm^{-1}}^{KBr}$ 3476, 3556(hydroxyl), 1774(γ-lactone). Recrystallization of the dibromide from chloroform-ether afforded colorless prisms elongated along c direction. This single crystal was then submitted to X-ray crystallographic analysis.

The crystal belongs to the monoclinic system. The following lattice parameters and space group were determined from the precession photographs of $0k\ell$, $k0\ell$ and $hk0$ layers using Cu$k\alpha$ radiation. $a = 10.28 \pm 0.01$, $b = 22.55 \pm 0.04$, $c = 8.19 \pm 0.01$ Å, $\beta = 113°10'$, $P2_1$. The crystal density measured by the flotation method using the mixture of carbon tetrachloride and methyl iodide was 1.65_3 g.cm^{-3} which corresponds to the calculated value of 1.62_2 g.cm^{-3} assuming four molecules of $C_{15}H_{22}O_4Br_2$ are contained in the unit cell. The crystal, therefore, contains two crystallographically unrelated molecules, A and B, in the asymmetric unit.

By visual estimation of the intensities, which was carried out by direct comparison with the standard scale, were obtained the relative intensity data of 1845 reflexions from the multiple film equi-inclination Weissenberg photographs of the layers $hk0$-$hk6$ about the c-axis and $h0\ell$-$h3\ell$ about the b-axis taken with Cu$k\alpha$ Radiation. The positions of the four bromine atoms were determined from the three-dimensional Patterson map. Using the bromine phases, the first three-dimensional Fourier synthesis was carried out. Six rounds of structure factor and Fourier calculations revealed out the well-defined electron density peaks corresponding to the very probable structures of the two molecules in the asymmetric unit. The atomic parameters of the both molecules so determined were then refined by the block-matrix least-squares calculations allowing the individual anisotropic thermal motions. The reliability factor at the present stage is 11.8%. The two independent molecules (A and B) in the asymmetric unit are in very similar conformation as shown in the crystal structure projected along the b-axis (Fig. 1). They are situated as if there were pseudo-twofold screw-axes lying parallel to the c-axis.

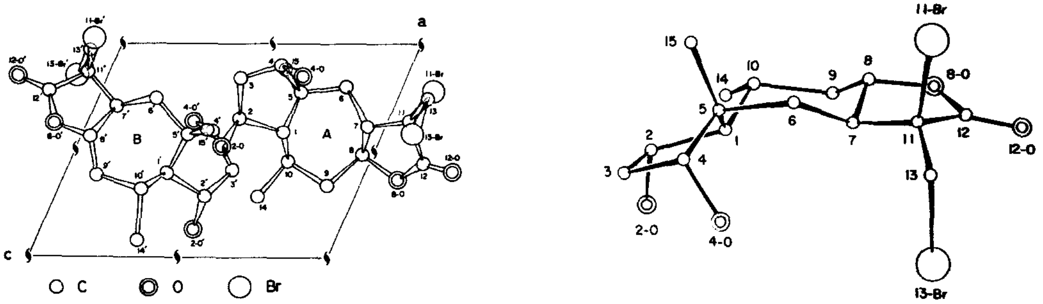

Fig. 1 Crystal structure of 11,13-dibromopulchellin(b-axis projection) and a perspective drawing of the molecule B viewed along $[0\ 1\ \overline{20}]$.

Measurements of the intensity differences caused by the anomalous dispersion of CuKα radiation by the bromine atom for ten pairs of $(hk\ell)$ and $(h\bar{k}\ell)$ reflexions, established the absolute stereochemistry of the molecule as follows: C_5- $\beta CH_3/C_1$- αH(trans ring juncture); C_7-αH /C_8- βH(trans γ-lactone); C_2- $\beta H/C_4$- βH(cis 1,3-diol); C_{10}- $\alpha CH_3/C_1$-αH(cis); C_{11}-αCH_2Br /C_7- αH(cis); C_{11}- $\beta Br/C_{13}$-Br(trans). Thus, the complete structure of the dibromide is illustrated by III, which directly proves the structures of pulchellin(II) and pulchellidine(I) in space except the rigid stereochemistry of the asymmetric centre at C_{11}(Fig. 2).

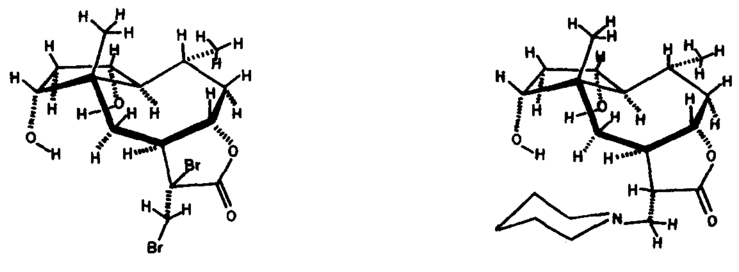

Fig. 2 Stereostructures of 11,13-dibromopulchellin and pulchellidine.

The flexible seven membered ring conformation of the molecule is forced to take a somewhat distorted flat chair, releasing non-bonded interactions between C_1-αH/C_7-αH and C_5-βCH_3/C_{10}-βH. The stereochemistry of C_{11}-$CH_2NC_5H_{10}$ side chain in pulchellidine(I), which was left unresolved by the present work, has been established as more stable configuration based upon stereospecific addition to II of piperidine(1)(2) like that of hydrogen(2) and of bromine mentioned above. Consequently, the absolute structures of pulchellidine and pulchellin have been independently established as designated in I and II, which are in full accordance with the conclusion obtained by chemical studies in the preceeding communication(2).

It is noteworthy to allude that the structure of pulchellin reveals the similar spacial situation to isotenulin(3).

Addendum:

While the manuscripts of the preceeding and present communications had been prepared, Prof. W. Herz informed by his private communication that pulchellin(II)(1)(2) possesses the same stereochemistry as II(5).

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