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ACUTUMINE AND ACUTUMIDINE, CHLORINE CONTAINING ALKALOIDS WITH A NOVEL SKELETON (1) : X-RAY ANALYSIS OF ACUTUMINE.

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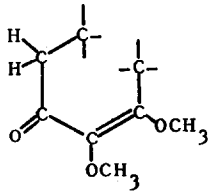
Acutumine is a minor alkaloid obtained[1] from Sinomenium acutum REHD. et WILS. (Japanese name: Oh-tsuzurafuji), a Menispermaceous plant, and its structure has long been unknown. Recently, we isolated acutumine from the same plant along with the N-nor base, for which we proposed the name acutumidine. Both alkaloids were also isolated from Menispermum dauricum DC. (Japanese name: Kohmori-kazura).

In early stage of the investigation, acutumine was reported to have the molecular formula $C_{20}H_{27}NO_8$ or $C_{21}H_{27}NO_8$[1]. After careful reexamination, however, we found that acutumine has a chlorine atom in the molecule and proposed the revised formula $C_{19}H_{24}NO_6Cl$ for acutumine[2].

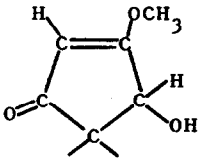
Acutumine, m.p. 238-240°(decomp.), pKa 5.3 (50% EtOH), $[\alpha]_D$ -206° (pyridine), shows IR ν_{max}^{Nujol} cm^{-1} 1690, 1670, 1625 (five- and six-membered conj. ketone system), 1605 (enol ether); NMR(pyridine) τ : 7.63 (3H, NCH_3), 6.28, 6.21, 5.96 (9H, $3xOCH_3$), 4.41, 4.99 (2H, 2xd., J= 0.8 cps, C<u>H</u>=C-C<u>H</u>-OH), 4.82 (1H, q., J= 7.5, 11 cps, CH_2-C<u>H</u>(Cl)); NMR(DMSO-d_6) τ : 3.86 (1H, d., J= 6 cps, HC-O<u>H</u>); UV λ_{max}^{EtOH} mμ 245 (ϵ 18970, five-membered conj. ketone), 270 (ϵ 9750, six-membered conj. ketone); MS m/e: 397 (M^+), 362 (M-35), 209 (base peak), 194, 181, 166, 150.

Acutumidine, m.p. 239-241°(decomp.), pKa 6.6 (50% EtOH), $[\alpha]_D$ -212° (pyridine), has a molecular formula $C_{18}H_{22}NO_6Cl$ and shows close similarity to acutumine in spectral properties. The interrelationship between them was established by the conversion of the former to the latter by N-methylation.

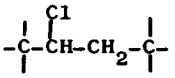
Presence of three partial structures (I, II and III) in these alkaloids are deduced on the basis of experimental evidences previously reported[2] and additional findings which will be discussed in the following communication.



I



II



III

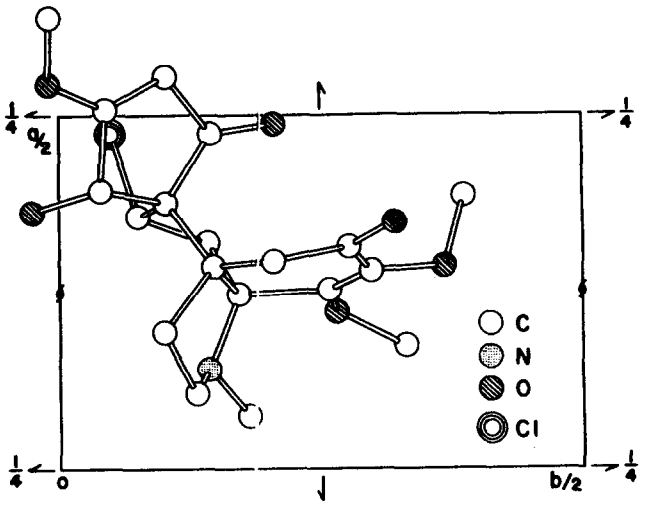
In parallel with further chemical investigation, X-ray analysis of acutumine was successfully performed. Now we wish to report the result of X-ray analysis in the present communication.

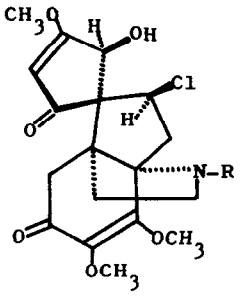
For the X-ray analysis, crystals of acutumine and acutumine acetate were prepared. The latter is monoclinic (space group, $P2_1$) with the unit cell containing four molecules (two per asymmetric unit) and though the chlorine atom coordinates had been determined from a three-dimensional Patterson synthesis, the elucidation of the positions of light atoms seemed to meet serious difficulties. Therefore, crystals of acutumine itself were chosen for the further analysis, in spite of the fairly small size of the specimens (0.07x0.07x0.25 mm).

The unit cell, which contains four molecules of the alkaloid, is orthorhombic, with parameters a=13.37, b=19.26 and c=7.22 A. Systematic extinctions of h00, 0k0 and 00l when h,k and l is odd, respectively, lead uniquely to the space group $P2_12_12_1$. Since intensities of reflections are weak on the average, diffraction measurements with a Hilger and Watts, Ltd., linear diffractometer (Mo Kα radiation) were carried out without filters except the equator, for which the measurements were repeated three times so as to minimize the counting error.

A three-dimensional sharpened Patterson function was calculated from

1459 independent data obtained. The three highest peaks (0.50, 0.41, 0.18), (0.05, 0.50, 0.32) and (0.45, 0.09, 0.50) in the three Harker sections H(1/2 vw), H(u 1/2 w) and H(uv 1/2), respectively, permitted the determination of probable coordinates of the chlorine atom as (0.025, 0.045, 0.090). The minimum function diagrams with four superposition calculated by the use of these chlorine coordinates were not clear cut. Nevertheless, fourteen maxima found in the diagrams seemed to be interpretable as atoms considering their peak shapes and heights and their relative arrangements in the unit cell. Starting with these tentative atomic positions, alternating applications of the least squares method and Fourier synthesis[3] (a technique employed for the elucidation of the structure of dihydroheliangine monochloroacetate[4]) revealed the structure of acutumine as shown in Fig. 1 or its mirror image.





Ia : R = CH_3

Ib : R = H

Fig. 1.

It was found, in this course, that four out of fourteen atomic positions assumed at first were inadequate. At the present stage, the R-value for 1116 data ($\sin^2\theta/\lambda^2 \leq 0.25$) is 0.138. There remains little ambiguity

concerning the identities of C, N, O atoms considering the peak heights in the Fourier map, temperature factors, bond lengths and angles and, especially, the chemical evidences which will be described in the following communication.

The calculation of structure factors taking the anomalous dispersion of Cl and O atoms into account indicated that intensities of certain pairs of reflections (hkl) and ($h\bar{k}l$) would differ by 20 %, if the Cu Kα radiation was used. Therefore, observed and calculated intensities of 29 of such pairs of reflections in the 1st and 2nd layers Weissenberg photographs were compared, from which the absolute configuration of the molecule was determined just as shown in Fig. 1. Thus the structure of acutumine and acutumidine can be represented by the formula Ia and Ib, respectively.

REFERENCES

1) K. Goto, H. Sudzuki, Bull. Chem. Soc. Japan, 4, 220 (1929).

2) K. Goto, M. Tomita, Y. Okamoto, Y. Sasaki, K. Matoba, Proc. Japan Acad., 42, 1181 (1966).

3) Detailed process will be published elsewhere.

4) M. Nishikawa, K. Kamiya, A. Takabatake, H. Oshio, Y. Tomiie, I. Nitta, Tetrahedron, 22, 3601 (1966).