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THE CRYSTAL STRUCTURE OF 16β-O-p-BROMOBENZOATE OF 6-KETO-LEUCOTYLIN

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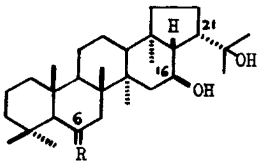
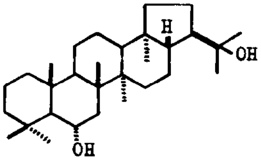
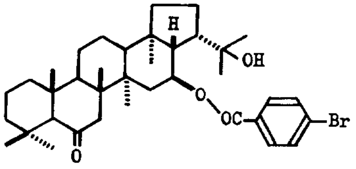
As described in the preceding paper1), it has become an important requisite to procure the defined depiction on the stereochemistry of leucotylin (I), isolated from a lichen Parmelia leucotyliza Nyl. along with zeorin (II) and leucotylic acid, since the stereochemical evidence found so far has suggested that the carbon skeletons of leucotylin and zeorin differ only at their C_{21} side chain and in addition the findings have appeared quite distinct from the biogenetic viewpoint, because the both triterpenoids have been found co-existing often in the lichen family.







I : R=β-H, α-OH, leucotylin
II : zeorin
III
IV : R=O, 6-keto-leucotylin

In the present study, the 16β-O-p-bromobenzoyl derivative (III) of 6-keto-leucotylin (IV) has been used for the X-ray diffraction analysis. The bromine derivative (III), mp. 235-8°; IR (KBr,cm^{-1}): 3505, 3456(OH group), 1705, 1704(sh)(C=O group), 1593(benzene ring), 1267 (-C-O-C=O group), ($CHCl_3$): 3518(OH group); 1703(C=O); 1594(benzene ring); 1260 (-C-O-C=O group); NMR (τ): 8.72, 8.78, 8.84, 8.91, 8.98, 9.06, 9.10, 9.16 (eight methyls), A^2B^2 type quartet (4H)(A^2 part at τ 2.16, J=8.2 cps. and B^2 part at τ 2.45, J=8.2 cps.), was obtained from 6-keto-leucotylin (prepared by CrO_3-pyridine oxidation of leucotylin) with p-bromobenzoyl chloride-pyridine. The retention of the carbon skeleton during the derivation was secured by recovering 6-keto-leucotylin from the bromo-derivative on alkaline hydrolysis of the latter, and also by the fact that the carbon skeleton of leucotylin has been found quite stable against mild alkaline condition.

The crystal structure of leucotylin has now been determined by a partial three dimensional X-ray study of the bromine derivative (III), $C_{37}H_{53}O_4Br$, M=641.7, which was crystallized from a mixture of ethanol and water. The crystal shape is the colorless orthorhombic plate. The unit-cell parameters measured on oscillation and Weissenberg photographs were found to be: a=12.03, b=44.06 and c=6.67 Å. Systematic absence of (h00) reflections for h odd and (0k0) reflections for k odd indicated $P2_12_12$ as the space group. The crystal density value of 1.25 g.cm^{-3} determined by the floatation method was best fitted by the assumption of four molecules and two water molecules in the unit cell. Intensity data of 1295 independent reflections were collected on an equi-inclination Weissenberg camera about the c axis at levels out to l=5. The intensities were estimated by visual comparison with a standard scale and were corrected with the appropriate Lorentz-polarization factors. No correction was made for absorption effects.

The structure was solved by the heavy atom method in three dimensions. The coordinates for bromine were obtained by locating the Br-Br peak on the three dimensional Patterson function. The phase calculated from the bromine position were then used for the first Fourier synthesis. The light atom peaks except isopropanol group could be identified unambiguosly, and the second Fourier synthesis using the phases of bromine and the identified light atoms revealed all the light atom coordinates. The structure was then refined by the block diagonal least-squares program on the HITAC 5020 Computer with individual isotropic temperature factors for all atoms. Fig. 1 shows the electron density map of a three dimensional contour projection looking down the c axis. The configuration of the molecule and the interatomic distances at the present stage of the calculation are shown in Figs. 2, 3, and 4, respectively. The R factor is 21% for observed term only and the average standard deviation in interatomic distances between light atoms is 0.07 Å. The Fourier map (Fig. 1) revealed that the bromine atom had a large anisotropic component of thermal vibration in the x direction. An anisotropic refinement for the bromine thermal parameters is now in progress, and by this procedure the R factor may be reduced more rapidly.

As indicated in Figs. 2, 3, and 4, the stereochemical structure of the A,B,C, and D rings and that of six quaternary methyl groups in III are identical with that proposed for hopane(2) and zeorin(3). However, the conformation of E ring of III has been disclosed to be in the so-called C_2 or "half-chair" form (Fig. 5a) rather than the Cs or "envelope" form (Fig. 5b), which has initially been destined to the E ring conformation of hopane derivatives(2). Furthermore, the most worthy to be mentioned is the finding that the isopropanol side chain at C_{21} is in α-quassi-equatorial orientation with the D/E juncture being trans-fused. Consequently, the isopropanol side chain at C_{21} of zeorin, which has

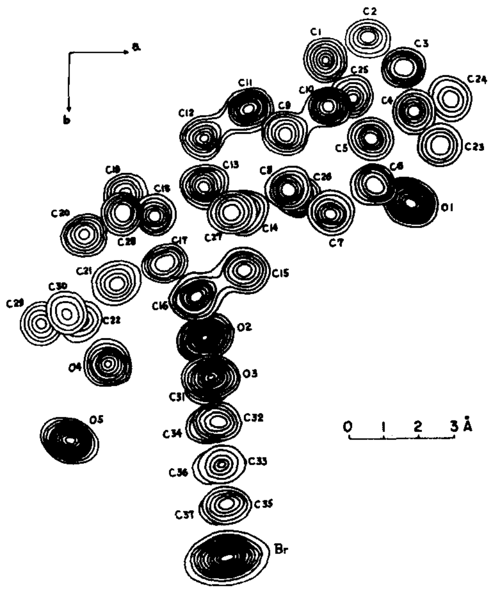
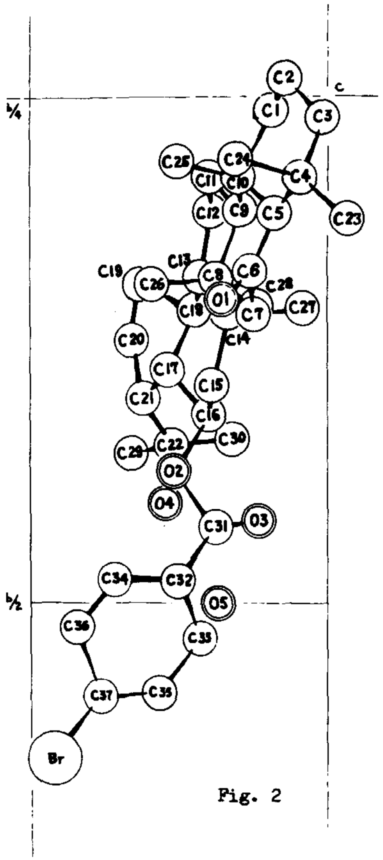

a
b
C1
C2
C3
C4
C5
C6
C7
C8
C9
C10
C11
C12
C13
C14
C15
C16
C17
C18
C19
C20
C21
C22
C23
C24
C25
C26
C27
C28
C29
C30
C31
C32
C33
C34
C35
C36
C37
O1
O2
O3
O4
O5
Br
0 1 2 3 Å

Fig. 1


c
b/4
b/2
C1
C2
C3
C4
C5
C6
C7
C8
C9
C10
C11
C12
C13
C14
C15
C16
C17
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C28
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C36
C37
O1
O2
O3
O4
O5
Br

Fig. 2

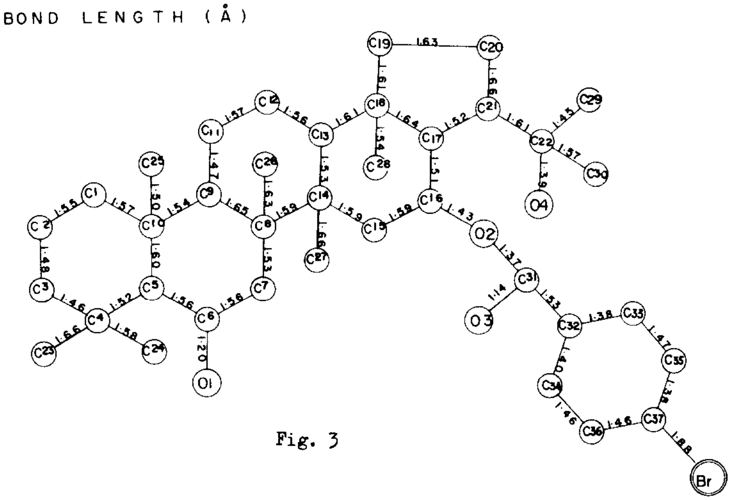
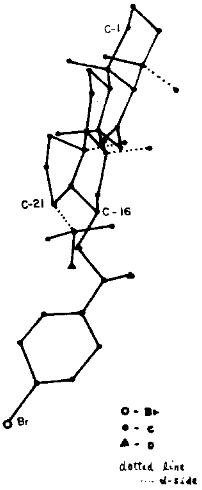


Fig. 3

Fig. 4



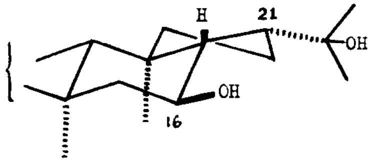


Fig. 5a

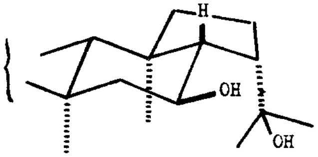


Fig. 5b

chemically been proved in the identical configuration with hopane[3)] and in the reverse against leucotylin[1)], should be expressed by the β-orientation (II), as proposed in the preceding paper[1)].

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References

1) I.Yosioka, T.Nakanishi, I.Kitagawa: the preceding paper.
2) G.U.Baddeley, T.G.Halsall, E.R.H.Jones: J.Chem.Soc., 1961 3891.
3) I.Yosioka, T.Nakanishi, I.Kitagawa: Chem.Pharm.Bull. (Tokyo), 15 353 (1967).
Y.Tsuda, K.Isobe, S.Fukushima, H.Ageta, K.Iwata: Tetrahedron Letters, 1967 23.