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THE STRUCTURE OF LEUCOTYLIC ACID,
A NEW TRITERPENIC ACID FROM A LICHEN

Itiro Yosioka, Tsutomu Nakanishi and Emako Tsuda
Faculty of Pharmaceutical Sciences, Osaka University
Toyonaka, Osaka, Japan

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Two triterpenic alcohols, zeorin and leucotylin, have been isolated from a lichen, Parmelia leucotyliza NYL., and their structures have been proposed to be Ia$^{1)}$ and Ib$^{2)}$ respectively. Further investigation of the above lichen, collected in the Kinki district of Japan, have enabled us to isolate a new triterpenic acid, now termed as leucotylic acid, along with zeorin and leucotylin. The yield of the acid varies depending upon the content of leucotylin in the lichen. The present communication concerns to the structure of leucotylic acid$^{3)}$.

Leucotylic acid (II), $C_{30}H_{50}O_4$, m.p. 260°, $[\alpha]_D$ +330° (c = 0.15, $CHCl_3$), exhibited hydroxyl (3200 cm^{-1}), and a carboxyl (1690 cm^{-1}) bands in the infrared spectrum (nujol), a positive Liebermann-Burchard color test, and negative property to tetranitromethane. On methylation with diazomethane, II gave methyl leucotylate (IIIa), $C_{29}H_{47}(OH)_2(COOCH_3)$, m.p. 298-301°, $^{\mathrm{nujol}}_{\mathrm{max}}$ 3200 (OH), 1720 cm^{-1} ($COOCH_3$) which showed seven singlets of methyls (τ: 9.22, 9.14, 9.01, 8.95, 8.84 (2 Me), 8.72) and one broad signal (5.88, 1 H) due to a proton attached to a carbon bearing a hydroxyl function in the NMR spectrum, suggesting one of eight methyls of a pentacyclic triterpene skeleton of II might be in an oxidized form of COOH and one of two hydroxyl functions could be secondary. Acetylation of

IIIa with pyridin-acetic anhydride at room temperature yielded smoothly monoacetyl methyl leucotylate (IIIb), $C_{29}H_{47}(OH)(OCOCH_3)(COOCH_3)$, m.p. 116°, ν_{max}^{nujol} 3555 (OH), 1730 ($COOCH_3$), 1755 cm^{-1} ($OCOCH_3$), with one hydroxyl group left unattacked. The NMR spectrum of IIIb indicated seven methyls (τ: 9.14 (2Me) 9.02 (1Me), 8.84 (4Me)), one acetoxylic methyl (τ: 7.94), and one proton signal (broad) centered at 4.8 ascribed to a hydrogen attached to a carbon with a secondary acetoxyl group.

When IIIa was treated with ethanolic hydrogen chloride as for the preparation of leucotylidiene from leucotylin[2], methyl leucotylidienate (IV), $C_{31}H_{48}O_2$, m.p. 203°; was obtained in about 50 % yield[*]. The physicochemical properties of the diene (IV) (ν_{max}^{nujol} 1720, 785, 775 cm^{-1}; λ_{max}^{EtOH} (log ε): 244 (4.29), 252 (4.32), 261 mμ (4.15); τ: 9.11 (2Me, s), 9.07 (Me, d, J = 7.2 cps), 8.98 (Me, d, J = 7.2 cps), 8.80 (2Me, s): AB quartet at 3.78, 4.42 (J = 10.8 cps, two olefinic proton)) indicate the similarity between the chromophores of monoacetyl leucotylidiene[2] and IV.

These findings along with the consideration of the probable common biogenetic origin of leucotylic acid, leucotylin and zeorin could agree to assume leucotylic acid having a hopane skeleton with two hydroxyl functions located at C-16 (secondary) and C-22 (tertiary) as in leucotylin (Ib).

Then our attention was focussed to establish the fundamental carbon skeleton of leucotylic acid.

On catalytic hydrogenation over Adam's catalyst, IV was transformed into a mono-ene mixture (V), $LiAlH_4$ reduction of V produced VIa, $C_{30}H_{50}O$, ν_{max}^{nujol} 3350 cm^{-1}, whose monoacetyl derivertive (VIb), $C_{32}H_{52}O_3$, exhibited absorption bands at 1742, 1238 cm^{-1} in the infrared spectrum (nujol), and AB quartet signals (2H) centered at τ 6.21 (J = 11 cps) due to $-\overset{|}{\underset{|}{C}}-C\underline{H}_2-OAc$ in the NMR spectrum. Chromic

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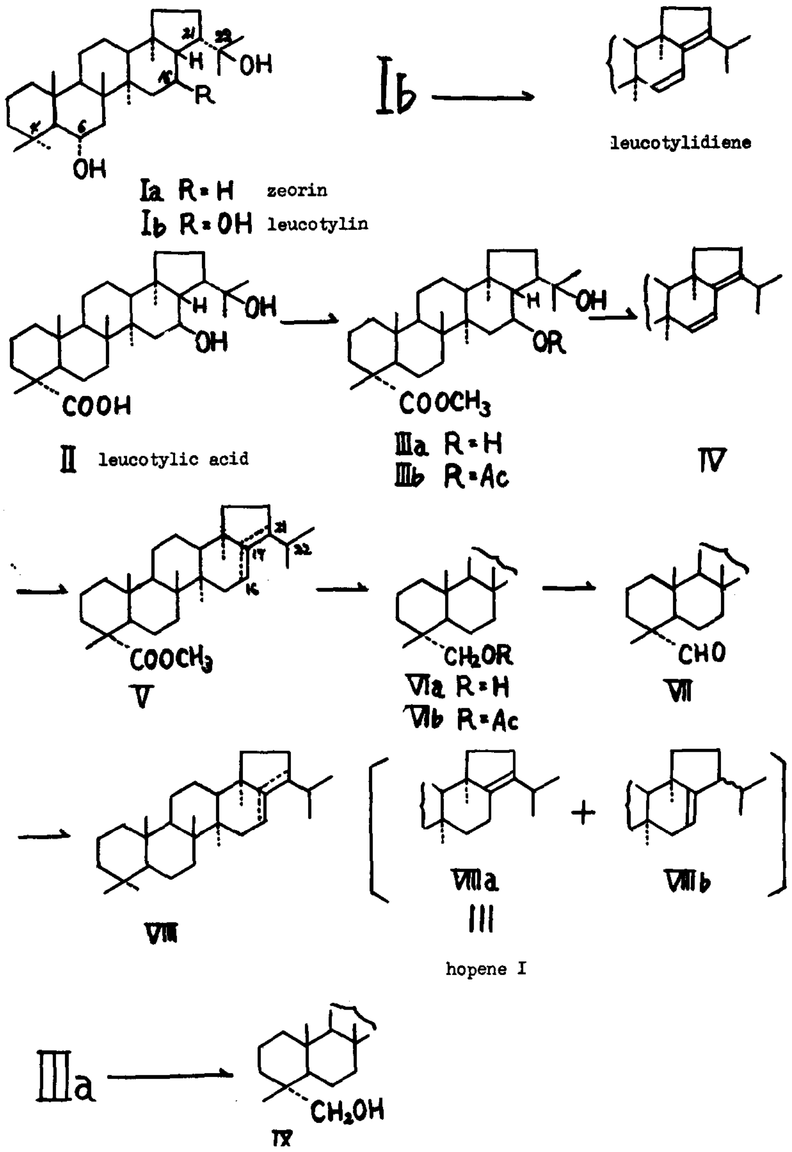
[*] Methyl isoleucotylate, $C_{31}H_{52}O_4$, m.p. 223°, an isomer of methyl leucotylate could be isolated as a by-product, which will be discussed in the forthcoming paper.


Ia R=H zeorin
Ib R=OH leucotylin
Ib
leucotylidiene
II leucotylic acid
IIIa R=H
IIIb R=Ac
IV
V
VIa R=H
VIb R=Ac
VII
VIII
VIIIa
VIIIb
hopene I
IIIa
IX
OH
R
COOH
COOCH3
OR
CH2OR
CHO
CH2OH

anhydride oxidation of VIa in acetic acid afforded an aldehyde (VII), $C_{30}H_{48}O$, ν_{max}^{nujol} 1724, 2646 cm^{-1} and subsequent Wölff-Kishner reduction of VII yielded a hydrocarbon mixture (VIII), $C_{30}H_{50}$, (colorless leaflets). Each reaction product from V through VIII has been found to consist of two components of double bond position isomers*) (corresponding probably to Δ^{16} and $\Delta^{17(21)}$). The final hydrocarbon mixture (VIII) was separated into two components of VIIIa, m.p. 181°, and VIIIb, m.p. 155° by using TLC (silica gel impregnated with $AgNO_3$). The former compound (lower Rf value on TLC) was proved to be identical with the authentic sample of hopene-I by mixed m.p., IR (KBr), GLC and TLC ($AgNO_3$) comparisons, thus confirming a gross structure of leucotylic acid having a hopane skeleton. The latter one with m.p. 155° could be assigned hopene-I isomer, presumably Δ^{16} compound (VIIIb), since NMR spectrum of VIb showed the diffused signal centered at 4.8 indicating an olefinic proton.

The NMR analyses (two methyl signals at τ 8.84, 8.72 of IIIa, 8.84 (2 Me) of IIIb) along with the above mentioned reaction sequence (from II through VIII via IV, analogous to leucotylin derivation[2)]) would agree to locate two hydroxyl functions at C-16 and C-22 respectively. Especially, the hydroxyl at C-16 could be designated as equatorial on the basis of easy acetylation, resistance for chromic anhydride oxidation and the diffused signal[4)] of the proton attached to C-16 in the NMR.

Finally, the location of a carboxyl group in leucotylic acid has been deduced to be at C-4 equatorial by the following evidences.

Several attempts aimed for lactonization or decarboxylation of leucotylic acid (II) or leucotylidienic acid (IV COOH instead of $COOCH_3$) were without success suggesting the carboxyl group located probably in ring A or B. On $LiAlH_4$ reduction, IIIa yielded a triol (IX), $C_{30}H_{52}O_3$, m.p. 246-7°, ν_{max}^{nujol} 3440, 3540 cm^{-1} (w), which exhibited in its NMR spectrum AB quartet signals centered at

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*) Probably formed by 1:2 or 1:4 addition of hydrogen to the parent hetero-annular diene (IV).

τ 6.74 (J = 10.5 cps). The comparison of methyl signals of zeorin[1a)] (Ia), leucotylin (Ib), methyl leucotylate (III) and the triol (IX) in the NMR spectra (TABLE I) reveals that one methyl signal ascribed to a methyl attached to ring A of IIIa or IX appeared at 8.84 or 9.13 whereas at 9.02, 9.04 in Ia, Ib respectively, supporting the location of carboxyl group in II at C-4 most probable[5)]. As mentioned above, AB quartet signals centered at τ 6.74 of IX, at 6.21 of VIb due to methylenes of CH_2OH and CH_2OAc respectively would support to assume an equatorial orientation (C-23) of CH_2OH in IX[4,6)].

TABLE I

(in τ value)

	18α	14α	8β	A-ring methyls (4α β, 10β)	C-22 gem. methyls
zeorin (Ia)	9.25	9.00	8.96	9.14 9.02 8.83*	8.83 8.83
leucotylin (Ib)	9.25	8.97	8.96	9.17 9.04 8.86*	8.78 8.86
Me-leucotylate (IIIa)	9.22	9.01	8.95	9.14 8.84	8.72 8.84
triol (IX)	9.25	8.98	8.90	9.23 9.13	8.73 8.83

* Deshielded by 6α-OH function[1b)].

Furthermore, pK_{mcs} value 7.80 of II has been found in good agreement with the calculated value[7)] (a-COOH 8.41, e-COOH 7.91) and a C-O-C streching absorption band of $COOCH_3$ in IIIa appearing at 1240 cm^{-1} could also corroborate for the equatorial configuration[8)].

All the compounds described here gave satisfactory analytical data.

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