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ON THE STEREOSTRUCTURES OF ZEORIN AND LEUCOTYLIN

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It was quite recently when the chemical proof of hopane skeleton of zeorin, a widely distributed triterpene alcohol in the lichen family, was accomplished[1,2]. As the carbon framework of hopane had already been elucidated by the previous workers as I[3], zeorin has been expressed by II[1,2]. On the other hand, the structure of leucotylin, a frequently coexisting triterpene with zeorin, has been proposed as III[4](having hopane skeleton) mostly based on its chemical behaviour and the biogenetic consideration.

However, on further investigation on the stereochemical correlation of these two triterpenes along with the X-ray analysis[5] of 16β-O-p-bromobenzoyl derivative (XXVII) of 6-keto-leucotylin (XXVI), we have reached to a conclusion that the structures of zeorin and leucotylin must be expressed by IV and V respectively and consequently hopane and isohopane (=moretane) should be revised to VI and VII contrary to the previous presentation[3,6]. In this communication, we wish to summarize our findings on these subjects*.

Leucotylin (V) —— On alkaline hydrolysis of 22-deoxyleucotylin diacetate (XI), derived from diacetyl-leucotylin (VIII) as described in the previous paper[7](via IX) and possessing the same carbon framework as leucotylin, a diol (XIII), $C_{30}H_{52}O_2$**, mp. 237.5-8.5°, IR**: 3440 cm^{-1}, was obtained. Chromic anhydride oxidation of the diol furnished a diketone (XIV), $C_{30}H_{48}O_2$, mp. 283-4°, IR: 1704, 1709 cm^{-1}, which was reduced with Na-isopropyl alcohol to the parent diol with the high yields in both reactions. The evidence supports to assign two equatorial secondary alcoholic functions in leucotylin (V). The broad NMR signal of 16β-O-acetyl-6-keto-leucotylin (XXVIII) appearing at 4.79 τ ($W_{\frac{1}{2}}$=18 cps.) ascribable to the axial proton at C_{16} also corroborates the assignment. The diketone (XIV) was found fairly stable against both acid and alkali, however, on refluxing in KOH-

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For the sake of simplicity, we use the new structure (IV and V) for the discussion hereafter.
** All the compounds quoted with the molecular formulae gave the satisfactory analytical values, and the IR spectra were taken in KBr unless stated otherwise.

ethyleneglycol, it was converted partly (less than 10%) to an isomeric diketone (XV), mp. 226-30°, IR: 1703, 1706 cm^{-1}, distinguishable from XIV by IR, TLC and GLC. The Huang-Minlon reduction* of XIV gave a monoketone (XVI), $C_{30}H_{50}O$, mp. 207-8°, IR: 1704 cm^{-1}, which is the key compound being able to correlate leucotylin (V) and zeorin (IV) as mentioned later.

An isomeric diol (XVII), $C_{30}H_{52}O_2$, mp. 251-3°, IR: 3580, 3480 cm^{-1}, prepared by the alkaline hydrolysis of XII[7] (derived via X) and having an epimeric isopropyl side chain at C_{21} against leucotylin skeleton, gave a diketone (XVIII), $C_{30}H_{48}O_2$, mp. 279-80°, IR: 1703, 1690 cm^{-1}, by CrO_3-AcOH oxidation in rather a low yield. The diketone in turn afforded a diol (XIX), $C_{30}H_{52}O_2$, mp. 234-5°, IR(nujol): 3411 cm^{-1}, a completely different alcohol from the aforementioned two diols, XIII and XVII. The fact that the diketone (XVIII) was reproduced quantitatively by CrO_3 oxidation of the diol (XIX), supports to assume the D/E cis juncture in XVIII, which probably was formed from the original trans fusion during the oxidation procedure**. The assumption can be supported by the finding that a monoketone (XX), mp. 156-8°, obtainable by the Huang-Minlon reduction of the diketone (XVIII), differs (distinguishable effectively on GLC) from two deoxyzeorinone derivatives. (XXIV,XXV)

Zeorin (IV) ——— 22-Deoxyzeorinone (XXIV), $C_{30}H_{50}O$, mp. 238-9°, IR: 1704 cm^{-1}, having the same C_{21} side chain configuration as zeorinone (XXI) and termed as α-deoxyzeorinone in the previous paper[1], was found to be non-identical (by virtue of mp., IR and TLC) with the monoketone (XVI) derived from leucotylin. While, another monoketone (XXV), $C_{30}H_{50}O$, mp. 204-7°, epimeric at C_{21} isopropyl configuration to zeorinone (XXI) and designated by β-deoxyzeorinone before[1], was proved identical with the monoketone (XVI) (mixed mp., IR, TLC, and GLC). These are the significant facts verifying that zeorin and leucotylin, although coexisting widely in the lichen family, possess the epimeric configuration at C_{21} in their carbon skeletons. As reported previously[1,2], the carbon skeleton of zeorin has chemically been demonstrated to be identical with hopane, therefore if one would assume the isohopane framework for leucotylin, all the evidence presented above could be fitted in a reasonable manner. However, as it seemed quite interesting from the biogenetic viewpoint that hopane and isohopane derivatives are coexisting in the lichen family, and furthermore it seemed worthwhile to have the solid answer on the carbon frameworks of these triterpenes, the X-ray analysis was performed on 16β-O-p-bromobenzoate (XXVII) of 6-keto-leucotylin (XXVI).

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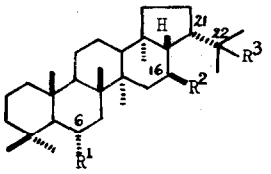
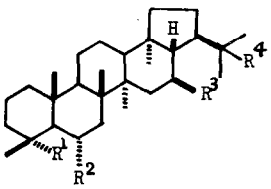
* The reduction was done by preparing hydrazone at first followed by the alkaline treatment to avoid the juncture isomerization during the procedure. The identity of XVI with XXV as described later indicates that in fact the isomerization of the D/E juncture did not occur.

** The ORD studies of these 16-keto derivatives (XIV, XV, XVIII) have been performed, and will be described in our full paper.

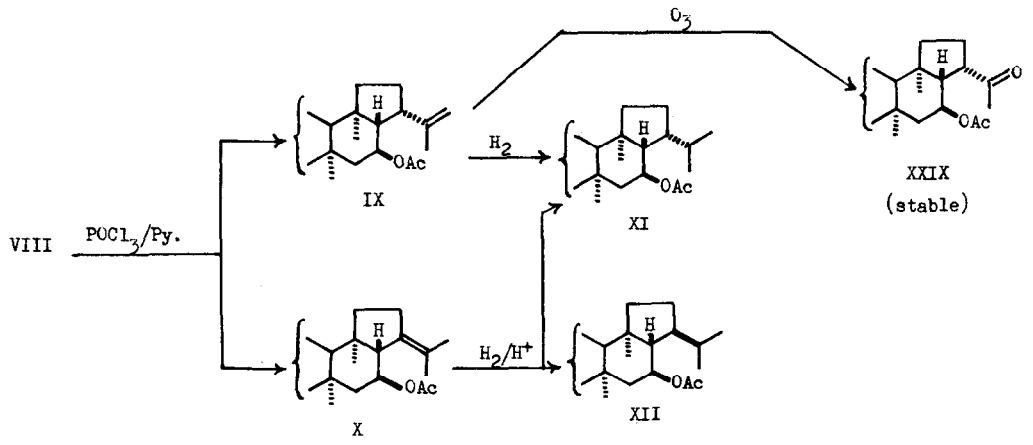
The satisfactory reason, why the ketone (XIV) having D/E trans juncture with C_{22} α side chain is less unstable comparing to the 16-keto derivative of XVII possessing D/E trans with C_{22} β side chain (easily isomerizable and not isolated yet), is still obscure and the problem is open to further study.

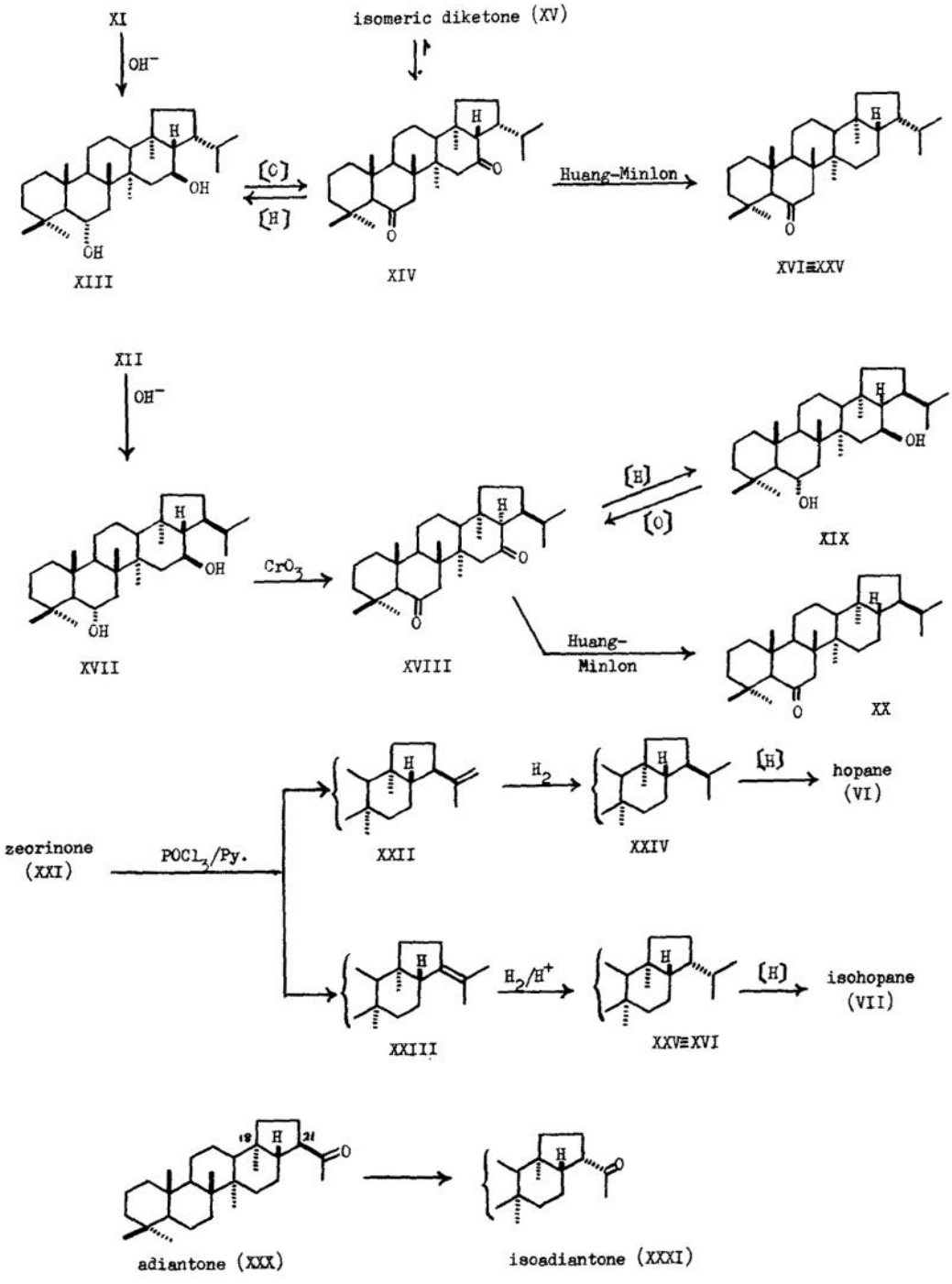


	R^1	R^2	R^3	
I	H	H	H	Proposed structures in previous papers
II	OH	H	OH	
III	OH	OH(	OH	
V	OH	OH	OH	= leucotylin
VII	H	H	H	= isohopane (= moretane)
VIII	OAc	OAc	OH	
XXVI	=O	OH	OH	
XXVII	=O	p-bromo-benzoyloxy-	OH	
XXVIII	=O	OAc	OH	



	R^1	R^2	R^3	R^4	
IV	CH_3	OH	H	OH	= zeorin
VI	CH_3	H	H	H	= hopane
XXI	CH_3	=O	H	OH	= zeorinone
XXXII	COOH	H	OH	OH	= leucotylic acid




XI
OH⁻
isomeric diketone (XV)
[O]
[H]
Huang-Minlon
XIII
XIV
XVI≡XXV
XII
OH⁻
CrO₃
[H]
[O]
XIX
XVII
XVIII
Huang-
Minlon
XX
zeorinone
(XXI)
POCl₃/Py.
XXII
H₂
XXIV
[H]
hopane
(VI)
XXIII
H₂/H⁺
XXV≡XVI
[H]
isohopane
(VII)
adiantone (XXX)
isoadiantone (XXXI)

Strikingly as will be postulated in the following paper[5], the p-bromobenzoate (XXVII) was clarified possessing an α quasi-equatorial C_{21} side chain attached to "C_2" form (half chair)[8] of ring E. This proves the structure of leucotylin being V and accordingly it follows that isohopane must be expressed by VII having α isopropyl function at C_{21} and in addition, zeorin and hopane by IV and VI with β oriented side chain at C_{21} contrary to the previous presentation.

Furthermore a norketone (XXIX), mp. 219-21°, IR: 1730 (broad), 1241 cm^{-1}, NMR ($CDCl_3$, τ): 7.85 (s, 3H), 7.97 (s, 3H), 8.07 (s, 3H) ($-\overset{|}{C}-OCC\underline{H}_3$ and $2\times -O-OCC\underline{H}_3$), prepared by O_3 oxidation of IX and retaining C_{21} configuration of leucotylin, was found stable against an acidic treatment*. Therefore, the significant instability of adiantone (now could be expressed by XXX and easily isomerizable to XXXI), approved previously due to the severe interaction between C_{18}-methyl and α-axial methyl ketone at C_{21}[3,9], would be accounted for either by its unstable β-axial character of the methyl ketone moiety attached to C_{21} of "C_2" form ring E (Fig.A.) or by the less stability of "C_s" form having a β-equatorial methyl ketone moiety (Fig.B.).

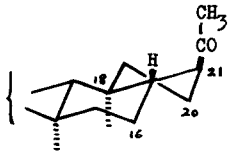


Fig. A.

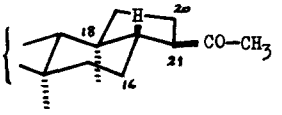


Fig. B.

There must be considerable strength of hydrogen bonding in the bromobenzoate (XXVII) between the hydroxyl function at C_{22} and the acyl function at C_{16}, and hence the association might cause somewhat conformational distortion especially in the D,E rings. To clarify the precise conformation of the D,E rings in hopane skeleton (lacking such an association), the X-ray analysis of a monobromobenzoyl derivative of 3,22-dihydroxyhopane is in progress in this faculty.

The revised structure XXXII for leucotylic acid, initially proposed as having α-hydroxy-isopropyl side chain at C_{21}[10], could reasonably be understood analogously by using the experimental evidences reported before[10,11]. The detailed discussion of which will be reported in future.

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* Ac_2O and AcOH were used to avoid hydrolysis of acetate groups similarly as for the the isomerization of a nor-derivative of methyl 16β-O-acetyl-leucotylate[10].

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