Tetrahedron Letters No.16, pp. 1161-1164, 1971. Pergamon Press. Printed in Great Britain.

REVISED STRUCTURE OF ZEORIN AND ITS CORRELATION WITH LEUCOTYLIN

Itiro Yosioka, Tsutomu Nakanishi, Hiroshi Yamauchi, and Isao Kitagawa
Faculty of Pharmaceutical Sciences, Osaka University
Toyonaka, Osaka, Japan

(Received in Japan 25 December 1970; received in UK for publication 19 March 1971)

Based on the chemical study$^{1)}$ and X-ray analysis$^{2)}$, the structure(I) was established for leucotylin, a lichen triterpenoid isolated from <u>Parmelia leucotyliza</u> Nyl. In addition, the chemical correlation between leucotylin and zeorin, a co-existing triterpenoid in the same lichen, has led us to propose$^{1,3)}$ the structure(II*)$^{4)}$ for the latter, possessing an isomeric isopropanol side chain configuration at C-21. Besides, the proposal has been extended to hopane as III* having C-21αH contrary to then believed structure(III, with C-21βH)$^{5)}$.

However, as mentioned in the preceding paper$^{6)}$, the structure of zeorin has been established as II with C-21βH configuration as same as leucotylin(I) and consequently it follows that hopane should be expressed as III, which coincides with the confirmation recently made X-ray crystallographically by Koyama and Nakai$^{7)}$. The conclusion is also in agreement with the chemical evidence supporting C-21βH of hopane presented by Ageta and Shiojima$^{8)}$.

These situations have led us to re-examine the experimental basis responsible for our previous presentation$^{1,3,4)}$, which is the subject of the present communication.

As shown in Chart 1, the correlation between leucotylin and zeorin was attained by preparing XI*(=XVI*) from both compounds. Especially of importance was that XI* was believed to hold C-21 configuration of leucotylin(I), which in turn brought out the assumption of C-21αH of zeorin(II*). Since zeorin has been clarified to possess actually C-21βH configuration by X-ray study$^{6)}$, there must be some discrepancy in the previous derivation either from leucotylin(I) to XI* or from zeorin to XVI*. As is presumed from the reaction sequence, the key discrepancy lies most likely in the assignment of IV*. The assumption has now been verified below.

Dehydration of 6-O-acetyl-zeorin(XVIII) using $POCl_3$-pyridine furnished an isopropenyl compound (XIX), $C_{32}H_{52}O_2$,$^{9)}$mp. 199-199.5°, IR$^{10)}$: 3080, 1740, 1253, 1643, 890, NMR: 8.22(3H, s), 5.17(2H, br. s), and an isopropylidene derivative(XX), $C_{32}H_{52}O_2$, mp. 123-123.5°, IR: 1738, 1250, NMR: 8.42(6H, s). An unstable norketone(XXI), $C_{31}H_{50}O_3$, mp. 219-221°, IR: 1734, 1712, 1246, NMR: 7.98, 7.90(3H each, s),

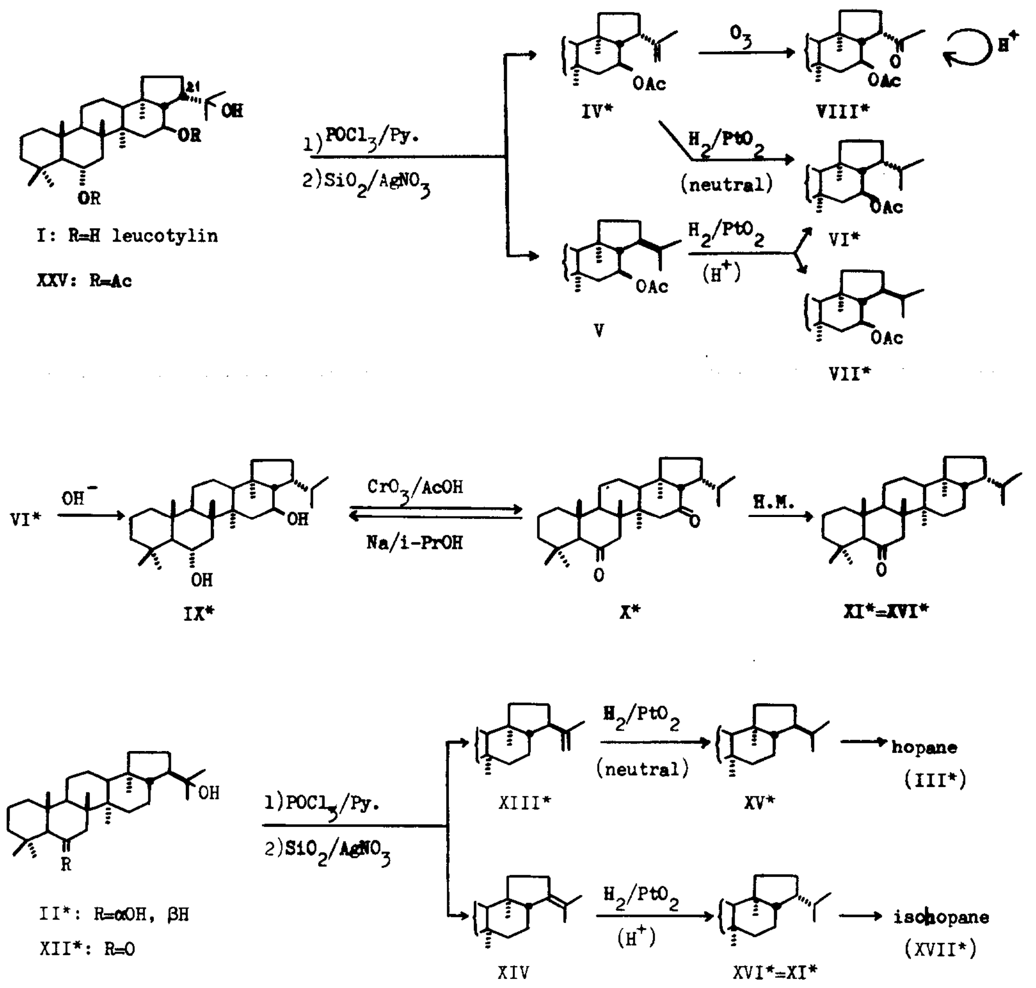

Chart 1: Previous assignment[1,3,4]

$[\theta]_{292}$ +4210(dioxane), was then obtained from XIX by ozonolysis and was easily isomerized on treatment with AcOH-Ac_2O to another norketone(XXII), $C_{31}H_{50}O_3$, mp. 224-226.5°, IR: 1735, 1714, 1246, NMR: 7.99, 7.88(3H each, s), $[\theta]_{292}$ +840(dioxane). These CD data are consistent with the published data of adiantone($[\theta]$ +4620) and isoadiantone($[\theta]$ +260)[11]. A monoketone(XXIV) derived from XIX via XXIII, $C_{32}H_{54}O_2$, mp. 181.5-183° through conventional route was identified with XV(previous assignment XV*), thus all the derivatives of zeorin including the previous experiment are elucidated as given in Chart 2. In other words, the previous assignment of C-21 configuration of XVI*(=XI*) should be inverted to XVI(=XI).

Treatment of di-O-acetyl-leucotylin(XXV) with $POCl_3$-pyridine followed by <u>rapid</u> separation

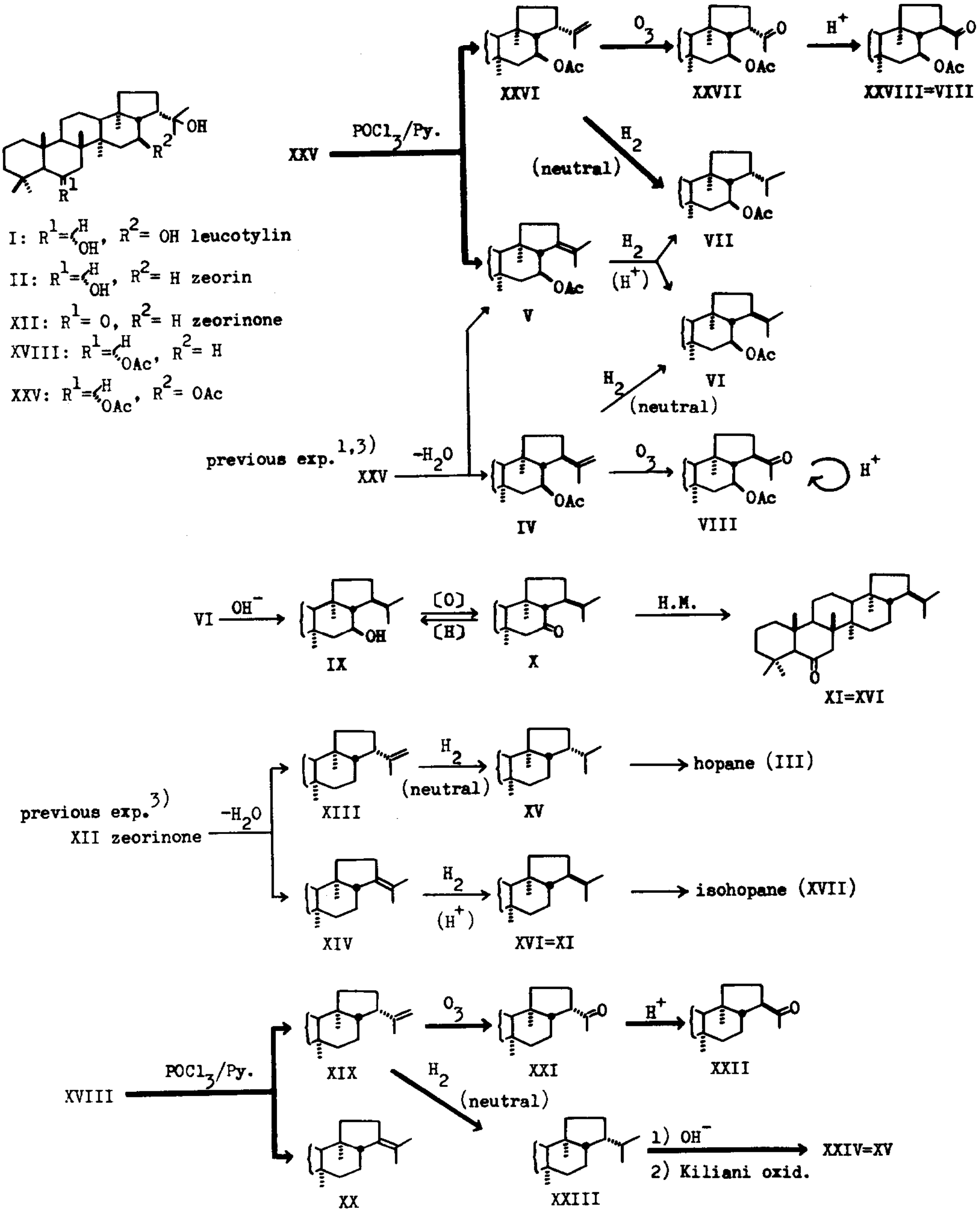

Chart 2: Established formulations of leucotylin and zeorin derivatives.
The derivations led with thick arrows indicate the present experiments.

using TLC(SiO_2-$AgNO_3$) furnished the isopropylidene compound(V) and a new isopropenyl derivative(XXVI), $C_{34}H_{54}O_4$, mp. 219-220°, IR: 1741(sh.), 1737, 1247, 1630(br), 890, NMR: 8.30(3H, s), 5.29(2H, br.s), which is completely distinguishable from the former isopropenyl derivative(now formulated IV). Hydrogenation of XXVI under neutral condition afforded VII being isomeric to another saturated compound(VI) derived from IV under the same condition.

Ozone oxidation of XXVI, on the other hand, gave a new unstable norketone(XXVII), $C_{33}H_{52}O_5$, mp. 229-230°, IR: 1740, 1725(sh), 1246, $[\theta]_{288}$ -2739(MeOH), which isomerized easily under acidic treatment to another norketone(XXVIII), mp. 218-221°, IR: 1740, 1725(sh), 1248, $[\theta]_{283}$ +2010(MeOH), identical with VIII(previous assignment VIII*)(mp., IR(KBr), ORD). These findings elucidate that the present norketone(XXVII) carries C-21βH configuration while VIII possesses C-21αH.

Accordingly, the correlation between leucotylin and zeorin is clarified in all respects as illustrated in Chart 2. We withdraw our earlier claim for the structures II*, III*, and XVII*. Surprisingly, the isopropenyl derivative(IV) was not holding the original C-21 configuration of leucotylin (I). It follows therefore that unexpected isomerization had occurred during the prolonged separation using SiO_2-$AgNO_3$ column in our previous experiment1) and the problem is further under investigation in this laboratory.

The authors would like to express their deepest thanks to the Res. Lab. of Dainippon Pharm. Co. for elementary analyses. One of the authors(H.Y.) wishes to express his sincere thankness to Japan Society for the Promotion of Science for the scholarship.

REFERENCES

1) I. Yosioka, T. Nakanishi, and I. Kitagawa: Chem. Pharm. Bull.(Tokyo), 17, 279(1969)(idem., Tetrahedron Letters, 1968, 1485).
2) T. Nakanishi, T. Fujiwara, and K. Tomita: Tetrahedron Letters, 1968, 1491.
3) I. Yosioka, T. Nakanishi, and I. Kitagawa: Chem. Pharm. Bull.(Tokyo), 17, 291(1969).
4) All the formulations numbered with asterisk(*) were erroneously made before as revealed in this paper. The correct structures are numbered without asterisk.
5) G.V.Baddeley, T.G.Halsall, E.R.H.Jones: J. Chem. Soc., 1961, 3891. Y.Tsuda, K.Isobe, S.Fukushima, H.Ageta, K.Iwata: Tetrahedron Letters, 1967, 23. Y. Tsuda, M.Hattori: Chem. Pharm. Bull.(Tokyo), 15, 1073(1967). R.E.Corbett, R.A.J.Smith, J. Chem. Soc.(C), 1967, 1622.
6) T. Nakanishi, H. Yamauchi, T. Fujiwara, and K. Tomita: Tetrahedron Letters, the preceding paper.
7) H. Koyama and H. Nakai: J. Chem. Soc.(B), 1970, 546.
8) H. Ageta and K. Shiojima: Chem. Comm., 1968, 1372.
9) All the new compounds with satisfactory analytical values are given with molecular formulae.
10) IR spectra were taken in CCl_4 unless specified otherwise and given in cm^{-1}. NMR data were taken in $CDCl_3$ and given in τ value.
11) P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry", Holden-Day, San Francisco, 1965, p. 145.