

ON CATALYTIC HYDROGENATION OF ANHYDROLEUCOTYLIN  
AND METHYL ANHYDROLEUCOTYLATE

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In previous papers, we have assigned the hopane skeletal structures, I and II respectively to leucotylin<sup>1)</sup> and leucotylic acid<sup>2)</sup> both isolated from a lichen, *Parmelia leucotyliza* NYL.. During the course of further studies on their chemical behavior, we have encountered some interesting facts mainly concerned with the catalytic hydrogenation of dehydration products (anhydro-leucotylin, and methyl anhydroleucotylate) obtained from acetyl derivatives of leucotylin and methyl leucotylate.

Thus, on treatment of leucotylin diacetate (III) with  $\text{POCl}_3$  in pyridine, there was obtained a mixture of double bond position isomers corresponding to hopene-a and -b types. Catalytic hydrogenation of this mixture with Adams' catalyst in  $\text{AcOH}$  and  $\text{AcOEt}$  afforded two saturated compounds, VI, m.p. 240-241°, and VII, m.p. 229-231°, separable by  $\text{Al}_2\text{O}_3$  column chromatography. Both compounds, VI and VII are also distinguishable on TLC and by their physical properties (IR, NMR).

To clarify the relation between these isomers, the separation of these double bond isomers were achieved by  $\text{AgNO}_3$  impregnated  $\text{SiO}_2$  column chromato-

graphy<sup>3</sup>), giving an isopropenyl derivative (IV),  $C_{34}H_{54}O_4^*$ , m.p. 210-211°; IR\*: 1730, 1240 (OAc), 1639 (C=C), 888 ( $>C=CH_2$ ); NMR\*: 5.36 (2H, s,  $>C=CH_2$ ), 8.28 (3H, s,  $>C=CH_2$ ), and an isopropylidene type compound (V),  $C_{34}H_{54}O_4$ , m.p. 182-183°; IR: 1727, 1242 (OAc); NMR: 8.38 (6H, s,  $>C=C(CH_3)_2$ ). Catalytic hydrogenation of IV in EtOH over Adams' catalyst yielded VI,  $C_{34}H_{56}O_4$ , m.p. 240-241°; IR: no absorption ascribable to double bond functions; NMR: total of eight methyls, between 8.89 and 9.25\*\*, as the sole product, which could be assigned as having an  $\alpha$ -isopropyl side chain at  $C_{21}$ . Similar catalytic hydrogenation of V in AcOH and AcOEt mixture\*\*\*, on the other hand, gave rise to VI and VII,  $C_{34}H_{56}O_4$ , m.p. 229-231°; NMR: eight methyls between 8.92 and 9.20; unexpectedly the latter was the major product. The side chain configuration of VII could be assumed to be  $\beta$ , isomeric with VI, based primarily on mechanistic consideration of its formation.

The following mechanism would account for this experimental evidence.

In an acidic medium, protonation on the isopropylidene double bond would take place at the beginning of the reaction, thus forming mainly cation (a) with the more stable  $\beta$ -oriented  $C_{21}$  side chain, and cation (b) with the less stable  $\alpha$ -oriented  $C_{21}$  side chain\*\*\*\*. The catalytic hydrogenation is then completed by hydrogen attack at each  $C_{22}$  cation center yielding VII (major) or VI\*\*\*\*\*. It has been accepted that in the hopane skeleton  $C_{21}$ - $\alpha$ -H epimer is more stable than the  $C_{21}$ - $\beta$ -H epimer<sup>4,5</sup>). Therefore, it follows that by virtue of product development control catalytic hydrogen attack on cation (a) would be more

\* Elementary analysis for all the samples described here was satisfactory. IR and NMR spectra were taken in  $CHCl_3$  or Nujol, and  $CDCl_3$  (at 60 Mc.), expressed in terms of  $cm^{-1}$  and  $\tau$  values, respectively.

\*\* Although the spectra of VI, VII, XIII, and XIV were run at 100 Mc, it was neither possible to assign the methyl signals to the respective methyl groups nor to deduce the J values of the isopropyl methyl groups.

\*\*\* Because of its tetrasubstituted character, the hydrogenation of V did not proceed smoothly without addition of AcOH.

\*\*\*\* Both cations could supposedly exist in equilibrium (probably in favor of (a)) via V.

\*\*\*\*\* An alternative route (less hindered  $\beta$  side, see V') of direct hydrogen attack at the double bond in V yielding VI can not be ruled out, although the product is apparently thermodynamically less stable.

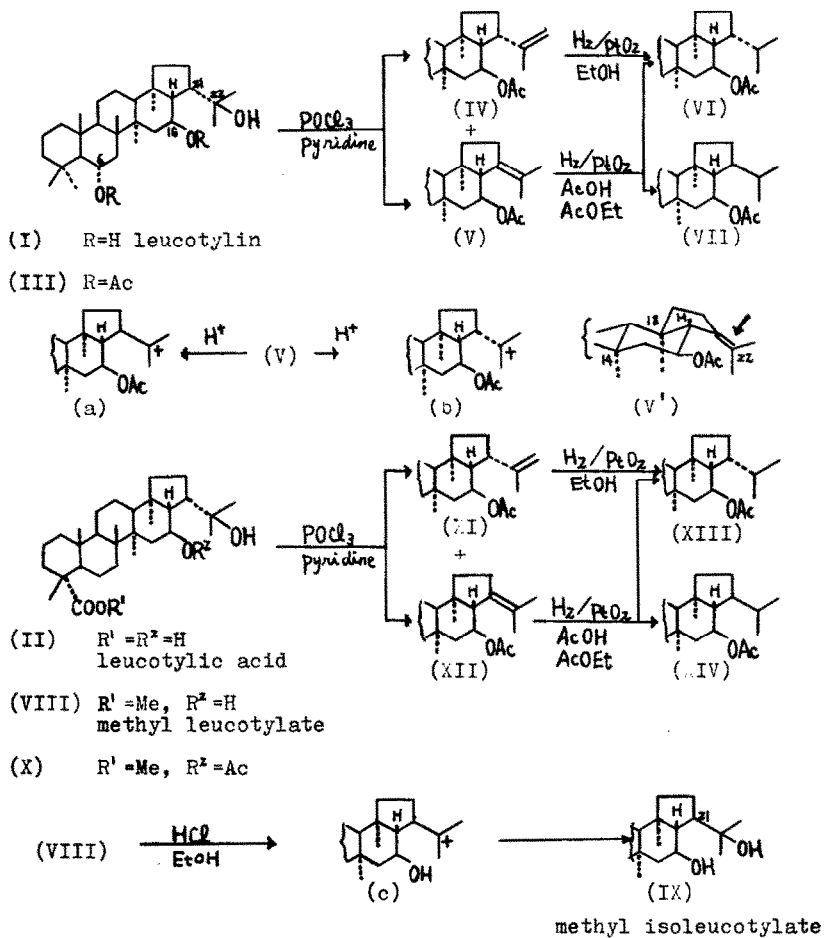
avored. The above mentioned intermediate ( $\alpha$ -type) could have analogously occurred as (c) in the acid catalysed isomerization of methyl leucotylate (VIII) to methyl isoleucotylate<sup>6</sup> (IX) (with  $\beta$  side chain at C<sub>21</sub>).

As would become of interest from the sequel, a similar investigation was performed on methyl anhydroleucotylate.

On treatment with POCl<sub>3</sub>-pyridine at room temperature, methyl 16-acetyl-leucotylate (X) furnished a mixture of anhydro derivatives, isopropenyl compound (XI), C<sub>33</sub>H<sub>52</sub>O<sub>4</sub>, m.p. 187.5-189°; IR: 1727, 1240 (OAc), 1648, 1623 (C=C), 892 (>C=CH<sub>2</sub>); NMR: 5.3 (2H, s, >C=CH<sub>2</sub>), 8.26 (3H, s, >C=C-CH<sub>3</sub>), and the isopropylidene isomer (XII), C<sub>33</sub>H<sub>52</sub>O<sub>4</sub>, m.p. 178-179.5°; IR: 1728, 1244 (OAc); NMR: 8.37 (6H, s, >C=C(CH<sub>3</sub>)<sub>2</sub>) in a ratio of 1 : 2, which could be separated by the aforementioned AgNO<sub>3</sub>-SiO<sub>2</sub> column chromatography. Catalytic hydrogenation of XI with PtO<sub>2</sub> in EtOH gave smoothly methyl deoxy-leucotylate (XIII), C<sub>33</sub>H<sub>54</sub>O<sub>4</sub>, m.p. 160-161°; IR: disappearance of absorptions due to C=C; NMR: seven methyls between 8.81 and 9.15, C<sub>21</sub> side chain of which must be  $\alpha$ -oriented. Similar hydrogenation of XII in AcOH and AcOEt, yielded another saturated derivative (XIV), C<sub>33</sub>H<sub>54</sub>O<sub>4</sub>, m.p. 208-210°; negative to tetranitromethane; NMR: seven methyls between 8.82 and 9.20, which could be obtained in a pure state by repeated recrystallization\* from methanol. The isopropyl side chain at C<sub>21</sub> in XIV could also be assigned  $\beta$  as for VII.

To shed further light on these anomalous hydrogenations, lichen triterpenoids with 22-hydroxyhopane skeletons including zeorin hitherto isolated in our laboratory are at present under study.

\* It has been found that  $\beta$ -side chain isomers are generally less soluble than the corresponding  $\alpha$ -isomers. The GLC study disclosed that the mother liquor of XIV contained mostly XIII.



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