

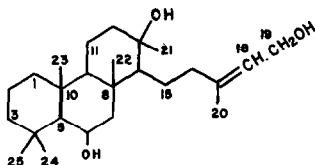
CHEILANTHATRIOL - A NEW FUNDAMENTAL TYPE IN  
SESTERTERPENES

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(Received in UK 20 September 1971; accepted for publication 15 October 1971)

THE long sought-after  $C_{25}$ -isoprenoids - the sesterterpenes - were discovered<sup>1</sup> only in 1965. Though, a number of sesterterpenes are known at present, only three skeletal types have been met with so far. We now report on the structure of cheilanthatriol (I), which represents a new fundamental type in sesterterpenes and provides a close analogy to the most common cyclisation encountered in triterpenes. We propose the name cheilanthane for the parent perhydro system.



The fern, Cheilanthus farinosa Kaulf. on extraction with pet. ether, yields, besides other substances, a crystalline triol, which we name Cheilanthatriol: m.p. 182-183°,  $[\alpha]_D^{25} +30.4$  (c, 1.2%) yield ~ 0.2% based on the whole plant.

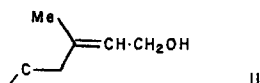
The compound analyses for  $C_{25}H_{44}O_3$  (no  $M^+$  ion;  $M^+ - H_2O$ ,  $m/e = 374$ ) and is clearly a triol [IR(KBr): OH 3450, 3360, 1125, 1075, 1055, 1003 and 990  $cm^{-1}$ ; no C=O absorption. Found: active H, 0.77%;  $C_{25}H_{41}(OH)_3$  requires: active H, 0.76%]. On exposure to  $Ac_2O$ -pyridine, it furnished a monoacetate (m.p. 123-124°. Mass:  $M^+$ ,  $m/e = 434$ ;  $M^+ - H_2O$ ,  $m/e = 416$ ;  $M^+ - 2 H_2O$ ,  $m/e = 398$ ;  $M^+ - AcOH$ ,  $m/e = 374$ ;  $M^+ - H_2O - AcOH$ ,  $m/e = 356$ ) at 0° after 5 min. or a diacetate [m.p. 83-84°. IR(KBr): OH 3530, 1031  $cm^{-1}$ ; OAc 1755, 1740, 1280, 1250  $cm^{-1}$ ] after 24 hr at room temp. (~25°), suggesting the primary and secondary character respectively of the concerned hydroxyls. This is clearly supported by the PMR ( $CDCl_3$ ) spectra of these compounds, which further disclose that the third hydroxyl must be tertiary: triol (3H overlapping signals at  $\delta$  3.5 - 4.3), monoacetate ( $CH_2OH$ , 1H broad triplet centred at  $\delta$  3.97,  $J = 11$  Hz;  $CH_2OAc$ , 2H unsymmetrical doublet further split by allylic coupling, centred at 4.65,  $J = 7$  Hz).

The triol shows in its PMR spectrum, one olefinic proton signal (1H, triplet centred at  $\delta$  5.48,  $J = 7$  Hz) indicating the presence of at least one ethylenic bond. On catalytic hydrogenation ( $PtO_2/AcOH$ ) it consumed ~ 2 mole equivalent of  $H_2$  to furnish as the major product, a saturated diol,  $C_{25}H_{46}O_2$  ( $M^+$ ,  $m/e = 378$ ), m.p. 192-193°, in

which the primary OH had been lost (FMR in  $\text{CDCl}_3$ :  $\text{CHOH}$ , 1H, triplet of doublets centred at  $\delta$  4.05,  $J_1 = 11$  Hz and  $J_2 = 3.5$  Hz; no  $\text{CH}_2\text{OH}$  or olefinic H signals). Thus, cheilanthatriol is mono-olefinic and being  $\text{C}_{25}\text{H}_{41}(\text{OH})_3$ , must be tricarbo-cyclic.

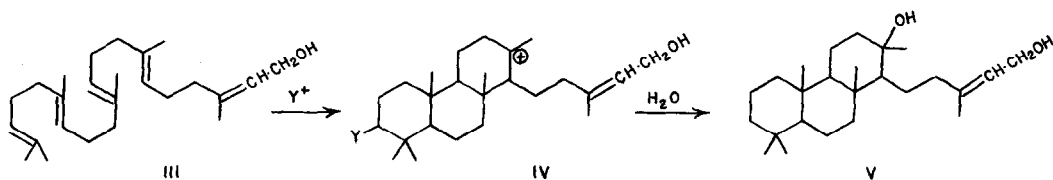
The PMR spectrum of cheilanthatriol also displays signals for five quaternary methyls (6H singlet at  $\delta$  0.86 and 3H singlets at  $\delta$  1.02, 1.12 and 1.16) and one vinylic Me (3H doublet at  $\delta$  1.80,  $J = 1.5$  Hz). This clearly indicates that cheilanthatriol is an isoprenoid and possibly a sesterterpene.

The triol on  $\text{MnO}_2$  oxidation furnished an aldehyde, m.p. 157-158°, displaying in its PMR( $\text{CDCl}_3$ ) spectrum  $\text{HC=O}$  signal as a 1H doublet centred at  $\delta$  9.9 ( $J = 8$  Hz) and the olefinic H as a doublet of quartets at  $\delta$  5.86 ( $J_1 = 8$  Hz,  $J_2 = 1$  Hz). This information coupled with the earlier PMR data and the results of catalytic hydrogenation clearly reveal the presence of unit II in cheilanthatriol.

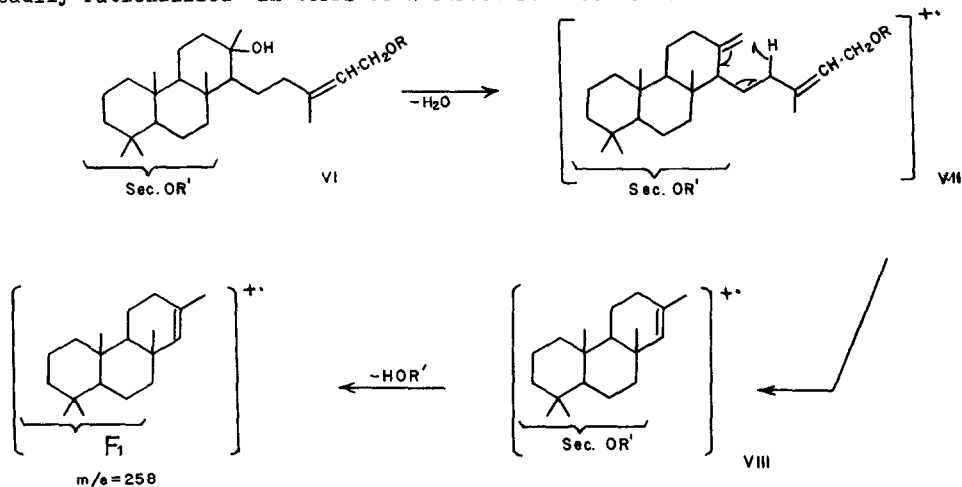


The structural features revealed so far make it clear that cheilanthatriol must be a sesterterpene and not a degraded triterpene. Furthermore, its genesis from geranylarnesol<sup>2</sup> (III; or its biological equivalent), the most plausible immediate precursor of sesterterpenes<sup>3</sup>, must involve cyclization onset at the isopropylidene end, so as to leave the part structure II (in geranylarnesol) intact. Such a cyclization can lead to the tricyclic species IV, singularly well-suited for structural requirements of cheilanthatriol. That Y (in IV) must be H and not OH is clear from the PMR splitting pattern of  $\text{CHOH}$  (triplet of doublets) in the hydrogenolysis product (saturated diol; *vide supra*) and a number of other derivatives, especially the unsaturated aldehyde from  $\text{MnO}_2$  reaction ( $\text{CHOH}$ , 1H, triplet of doublets centred at  $\delta$  4.0,  $J_1 = 11$  Hz,  $J_2 = 4$  Hz), as this pattern can arise only from an ABCX system<sup>4</sup> and not from an ABX system (which will be the case if Y in IV were OH). Thus, IV can lead to V, which by biological oxidation can incorporate a secondary hydroxyl. Such a structure can meet all the structural requirements of cheilanthatriol, disclosed so far.

Support for the perhydrophenanthrene skeleton and the positions of the non-angular methyls and the side-chain was forthcoming from the Se-dehydrogenation (310-340°, 48 hr) of the triol, when 1,7-dimethylphenanthrene (minor) and 1,7,8-trimethylphenanthrene (major) were obtained and identified by m.p., (m.p. of TNB complexes), UV absorption and mass spectra.



The disposition of the side-chain with respect to the tertiary hydroxyl, as depicted in V, received support from the results of electron impact. Cheillanthatriol, its monoacetate and its diacetate, all fragment to the same ion at  $m/e = 258$  (base peak in the case of mono- and diacetate and, 65% intensity in the case of triol). This is readily rationalised<sup>5</sup> in terms of a structure based on V:

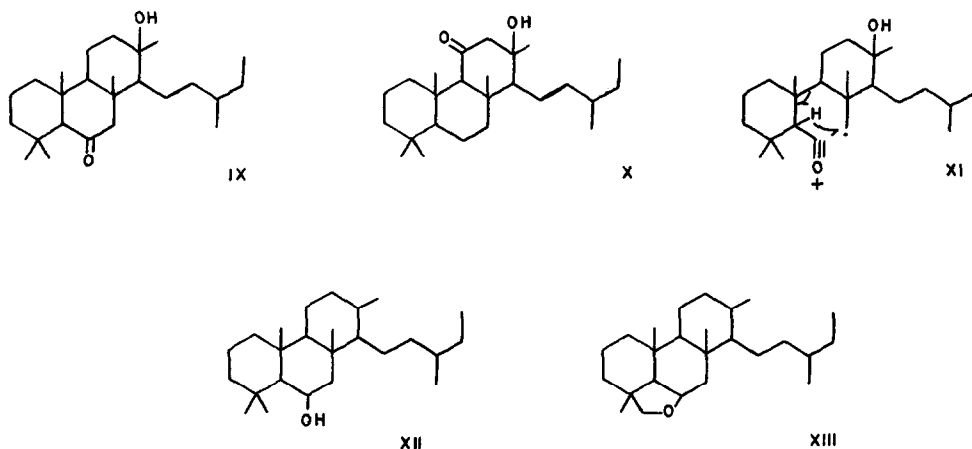


In support of this both triol (17%) and mono-acetate (45%) show ions at  $m/e = 276$  (VIII,  $R'=H$ ) and metastable ions at  $\sim 241$  (calcd. 241.1).

The above fragmentation also clearly shows that the secondary hydroxyl must be located on a ring. As indicated earlier, this hydroxyl function must be flanked by three vicinal hydrogens and the splitting observed clearly indicates two diaxial ( $J = 11$  Hz) and one axial-equatorial ( $J = 4$  Hz) couplings<sup>6</sup>. Thus, this secondary OH must be equatorial and can be located at either  $C_6$  or  $C_{11}$ . Evidence in favour of  $C_6$ -OH was arrived at as follows.

The saturated diol obtained by hydrogenolysis on Sarett oxidation<sup>7</sup> furnished a keto alcohol [m.p. 115-116°. IR(Nujol): OH  $3435\text{ cm}^{-1}$ ; C=O  $1700\text{ cm}^{-1}$ ], which in view of the previous discussion can be IX or X. Since this keto alcohol was found to be stable in alkaline medium, possibility X can be eliminated. Structure IX is also clearly supported by its mass fragmentation. Thus, for example ion at  $m/e = 151$  (100%) is readily understood in terms of XI and, the  $m/e = 151$  ion giving  $m/e = 123$  ion (75%) by CO elimination.

Thus, cheillanthatriol can reasonably be considered to have the gross structure I. Further work to correlate it with a compound of well-established absolute stereochemistry is underway. In another series of experiments, the hydrogenolysis diol was ultimately converted into XII (m.p. 168-172.  $M^+$ ,  $m/e = 362$ ) which on treatment with  $Pb(OAc)_4-I_2 (h\nu)$ <sup>8</sup> was quantitatively converted into a cyclic ether (m.p. 105-107°.  $M^+$ ,  $m/e = 360$ ), which in view of its PMR spectral characteristics must be formulated



as XIII. This facile cyclization, coupled with the spin-spin coupling of the  $C_6$ -proton (*vide supra*), besides confirming gross structure I would suggest trans-anti-trans backbone.

Acknowledgement - The A.M.U. group wishes to acknowledge financial assistance from the Ministry of Health, Govt. of India.

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