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RETIGERANIC ACID , A NOVEL SESTERTERPENE ISOLATED FROM THE LICHENS OF LOBARIA RETIGERA GROUP

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Previously we reported the occurrence of new migrated hopane-type triterpenes, retigeric acids A and B, in some lichens of Lobaria retigera group, and established their structures as 2α,3β-dihydroxyfern-9(11)-en-23-oic acid and 2α,3β-dihydroxyfern-9(11)-en-23,25-dioic acid, respectively.[1,2] In addition to these triterpenes we isolated a new compound, m.p. 221-222°, $[\alpha]_D^{18}$ - 99.2° ($CHCl_3$), tentatively named compound L-A, from Lobaria isidiosa (Müll.Arg.)Vain. var. subisidiosa Asah. (= L. isidiosa (Müll.Arg.)Vain. by Yoshimura[3]) collected in the eastern Himalayas, Bhutan, while it was also found in L. subretigera Inum. (L. pseudopulmonaria Gyeln. by Yoshimura[3]) by TLC.

The physical properties of compound L-A resembled closely those of retigeranic acid, $C_{24}H_{38}O_2$, m.p. 218-221°, $[\alpha]_D^{23}$ - 59° ($CHCl_3$) , isolated by Seshadri et al.[4] from the lichens of L. retigera group collected in the western Himalayas. The identity of compound L-A with retigeranic acid has been established by a mixed fusion and comparisons of TLC and IR spectra.

Retigeranic acid (I) which gave a positive tetranitromethane reaction and a negative Liebermann-Burchard reaction was obtained from the chloroform-soluble fraction of the ethereal extracts of the lichen. The molecular formula has now been revised to $C_{25}H_{38}O_2$ by the accurate mass spectrometry (M^+ calcd. for $C_{25}H_{38}O_2$: 370.287 ; found: 370.286). The IR spectrum (in KBr) gave absorptions at 1662 and 1608 cm^{-1}, the UV spectrum showed an absorption at 242 nm(log ε 3.91) and the mass spectrum gave peaks at m/e 370 (M^+) and 325 (M - COOH). These spectral data revealed that retigeranic acid is a sesterterpene having an αβ-unsaturated carboxyl group. The NMR spectrum indicated the presence of five C-Me groups, of which two are tertiary[**] and the rest are secondary, and gave no signals of olefinic protons.

The above results suggested that retigeranic acid has no close structural correlation with

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[**] Singlets (δ 0.80 and 1.01 , in d_5-pyridine)

the sesterterpenes hitherto known[5-9], but did not provide any tenable evidences for its skeletal structure.

We undertook, therefore, an X-ray structure analysis with the heavy atom method using retigeranic acid p-bromoanilide, $C_{31}H_{42}NOBr$, m.p. 276-278° (II). Recrystallization from acetone solution affords colourless monoclinic crystals elongated along the b-axis giving the unit cell dimensions of $a = 13.14_2$ Å, $b = 9.37_7$ Å, $c = 11.49_8$ Å, $\beta = 102.4_1$ ° and the space group $P2_1$, D_x : 1.262 $g.cm^{-3}$, D_m : 1.254 $g.cm^{-3}$ (in hexane and CCl_4) with two molecules in the unit cell. Precise lattice constants and three dimensional diffracted intensities were derived from the measurements using a Rigaku computer controlled 4 circle diffractometer. A total of 1639 independent reflexions were measured with CuKα radiation, and 818 independent reflexions including Friedel pairs with MoKα radiation. The position of bromine atom was determined by a sharpened Patterson synthesis, and then Fourier synthesis was carried out using the phases determined by the anomalous dispersion method in order to avoid the appearance of a mirror image on the Fourier map. Successive use of Fourier and difference Fourier syntheses enabled us to assign the structure for this compound.

Refinement of the structural parameters was made by repeated cycles of the block-matrix least-squares calculations. Anisotropic thermal parameters were allowed for each atom. The final R-value was 0.094. The molecular structure of II determined by the present X-ray analysis is shown in Fig 1, which is drawn with correct absolute configuration.

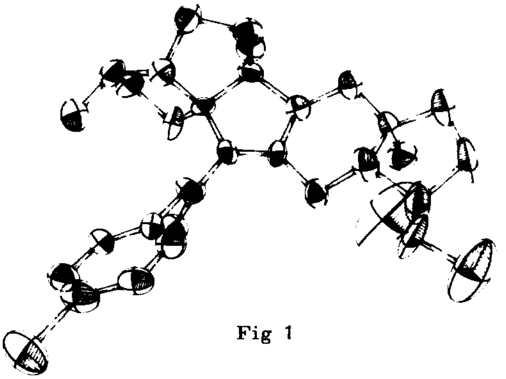
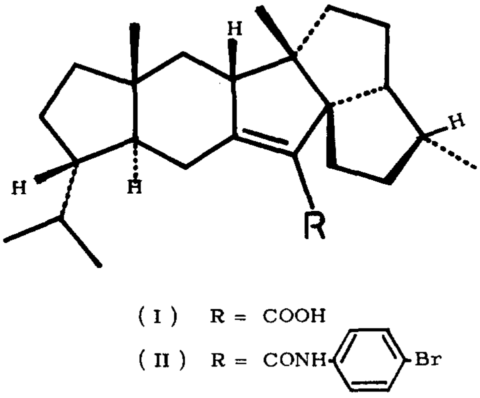
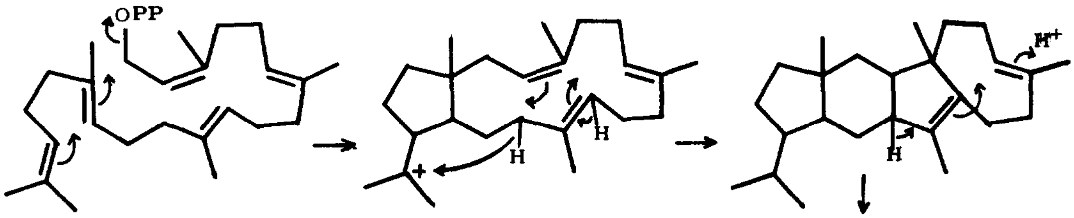


Fig 1



Consequently, the structure of retigeranic acid including its absolute configuration has been established as(I).

This unique pentacyclic sesterterpene could be constructed biogenetically by the cyclization of geranylfarnesyl pyrophosphate as shown below. Retigeranic acid (I) is notable also as the first sesterterpene occurring in lichens.



(I)

The full details of the present X-ray crystallographic study will be reported elsewhere.

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