Structure of (−)-Neoverrucosan-5β-ol, a Diterpenoid from *Mylia verrucosa* (Liverwort) containing a Novel Carbon Skeleton: *X*-Ray Crystal and Molecular Structure of the Benzoate

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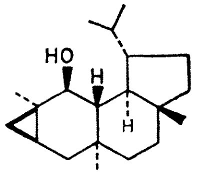
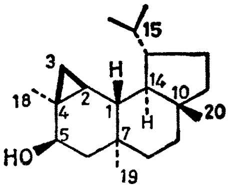
Summary The structure and absolute configuration of a novel diterpene alcohol, (−)-neoverrucosan-5β-ol, isolated from the liverwort *Mylia verrucosa* has been shown to be (**2**) on the basis of chemical and spectral evidence and *X*-ray analysis of the benzoate (**6**).

PREVIOUSLY, we have isolated (−)-2β-hydroxyverrucosane (**1**) and five related diterpenoids with a verrucosane skeleton from the liverwort *Mylia verrucosa* Lindb. and their structures, including absolute configuration, have been determined by extensive chemical reactions and spectral data.[1-3] The novel verrucosane skeleton has been recently confirmed by *X*-ray analysis of the mono-*p*-bromobenzoate of the major diol.[4] In continuing research on chemical constituents of the liverwort, we have isolated a further diterpene alcohol, (−)-neoverrucosan-5β-ol (**2**), containing a novel carbon skeleton† from the ethanolic extract by means of column chromatography and preparative t.l.c. We describe here not only the structure and absolute configuration of the novel alcohol (**2**), but also its acid-catalysed reaction which gives (+)-homoverrucosan-5β-ol (**7**).

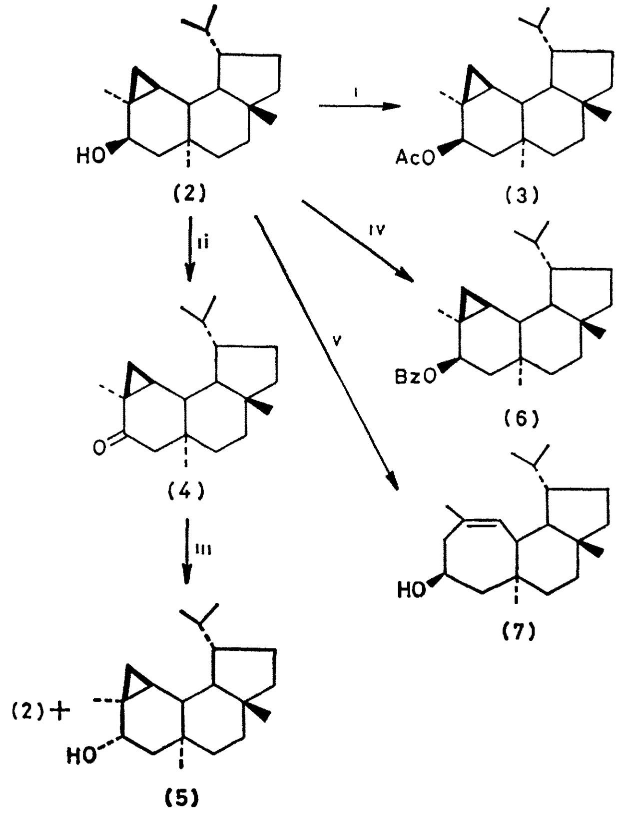


(**1**)



(**2**)

The i.r. and ^{1}H n.m.r. spectra‡ of the compound (**2**), $C_{20}H_{34}O$, m.p. 174—175 °C, $[\alpha]_D$ −10°, revealed that it was a saturated tetracyclic diterpenoid containing a cyclopropane ring [ν 3060 cm^{-1}, δ 0·2—0·7 (2H, m)], an isopropyl group [ν 1380 and 1373 cm^{-1}, δ 0·81 and 0·88 (each 3H, d, J = 5·5 Hz)], 3 tertiary methyls [δ 0·73, 0·82, and 1·17 (each 3H, s)], and a secondary hydroxy group [ν 3270 cm^{-1}, δ 4·01 (1H, dd, J = 7·0 and 4·5 Hz)], the presence of which was confirmed by formation of the acetate (**3**), $C_{22}H_{36}O_2$, m.p. 127·5—129 °C, $[\alpha]_D$ −6°. Jones reagent oxidized the alcohol (**2**) to the ketone (**4**), $C_{20}H_{32}O$, m.p. 67·5—68 °C, $[\alpha]_D$ +140°. It had a carbonyl group (6-membered ketone) conjugated with the cyclopropane ring [ν 1670 cm^{-1}] and a methylene adjacent to a quarternary carbon atom [ν 1435 cm^{-1}, δ 1·87 and 2·06 (each 1H, d, J 15·0 Hz)]. The ketone (**4**) was then reduced with $NaBH_4$ to afford the original alcohol (**2**) and its epimer (**5**), $C_{20}H_{34}O$, m.p. 121—122 °C, $[\alpha]_D$ −52°, in a ratio of 2 : 5. This chemical evidence and the similarity of the spectra with those of verrucosanol (**1**) and its derivatives suggested that the overall structure might be represented by (**2**).



Reagents: i, Ac_2O in pyridine; ii, CrO_3 in H_2SO_4–acetone; iii, $NaBH_4$ in EtOH; iv, PhCOCl in pyridine; v, 0·5 N H_2SO_4 in acetone (1 : 5).

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† We propose the name neoverrucosane for the new carbon skeleton from its connection with the verrucosane skeleton, and suggest the numbering shown in (**2**).

‡ I.r. and ^{1}H n.m.r. spectra were, respectively, determined for KBr pellets and $CDCl_3$ solution, and optical rotations for $CHCl_3$ solution. All new compounds (**2**)—(**6**) gave spectral data in good agreement with the assigned structures.

In order to confirm the structure and stereochemistry, the alcohol (**2**) was transformed into the benzoate (**6**), $C_{27}H_{36}O_2$, m.p. 148·5—150 °C, $[\alpha]_D + 13°$, colourless orthorhombic crystals, and an *X*-ray analysis of the benzoate was carried out.

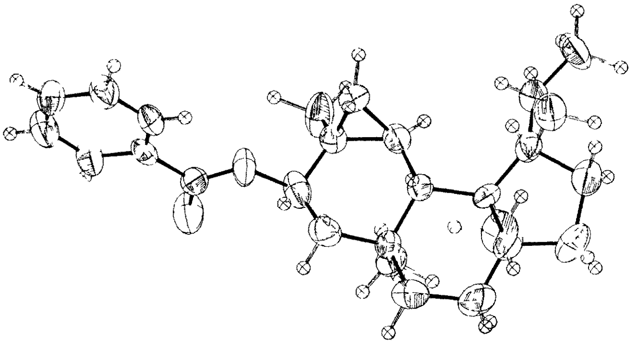

FIGURE. A computer-generated perspective drawing of the benzoate (**6**).

Crystal data: $a = 6{\cdot}278(2)$, $b = 9{\cdot}971(6)$, $c = 37{\cdot}451(26)$ Å, space group $P2_12_12_1$, $D_c = 1{\cdot}12$, $D_m = 1{\cdot}12$ g cm^{-3} (in $ZnCl_2$), $Z = 4$. The diffraction intensities were collected in the ω scan mode using graphite-monochromated Mo-K_α radiation on a Syntex *R*3 automatic diffractometer. 2235 independent reflections were measured, and 1200 were judged to be observed after correction for Lorentz, polarization, and background effects. The structure was solved by direct methods using MULTAN in the Syntex XTL program. Refinement by full-matrix least-squares, using anisotropic thermal parameters for the non-hydrogen atoms and isotropic ones for the hydrogen atoms excluding those of the five methyl groups, converged to a current *R*-value of 0·067.§ The structure, excluding the absolute configuration, of the benzoate (**6**) is shown in the Figure. By analysis of the c.d. spectrum ($[\theta]_{285}$ +11,750 and $[\theta]_{213}$ +18,700 in MeOH; $[\theta]_{292}$ +9,620 and $[\theta]_{202}$ +21,900 in iso-octane) of the cyclopropyl ketone (**4**),[5] the absolute configuration was then established as (**2**).

The alcohol (**2**) contains a novel fused 3,6,6,5-tetracyclic ring system in the *cis-trans-anti-trans*-configuration, and the hydroxy group is *cis* to the cyclopropane ring.

When the cyclopropyl alcohol (**2**) was treated with acid, it was converted in good yield into the homoallyl alcohol (**7**), $C_{20}H_{34}O$, m.p. 153—154 °C, $[\alpha]_D$ +17°, which was identical with (+)-homoverrucosan-5β-ol obtained by the same acid treatment of (−)-verrucosanol (**1**).[3]

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§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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