Structure of (−)-2,9-Dihydroxyverrucosane, a Novel Carbon Skeletal Diterpenoid from the Liverwort *Mylia verrucosa*

By AKIHIKO MATSUO,* HIROSHI NOZAKI, MITSURU NAKAYAMA, and SHÛICHI HAYASHI*
(*Department of Chemistry, Faculty of Science, Hiroshima University, Hiroshima* 730, *Japan*)
and DAISUKE TAKAOKA
(*Department of Chemistry, Faculty of Science, Ehime University, Matsuyama* 790, *Japan*)

Summary A novel carbon skeletal diterpene diol isolated from the liverwort *Mylia verrucosa* has been shown to have the structure (**1**), containing a novel fused 3,6,6,5-tetracyclic ring system, on the basis of chemical and spectral evidence.

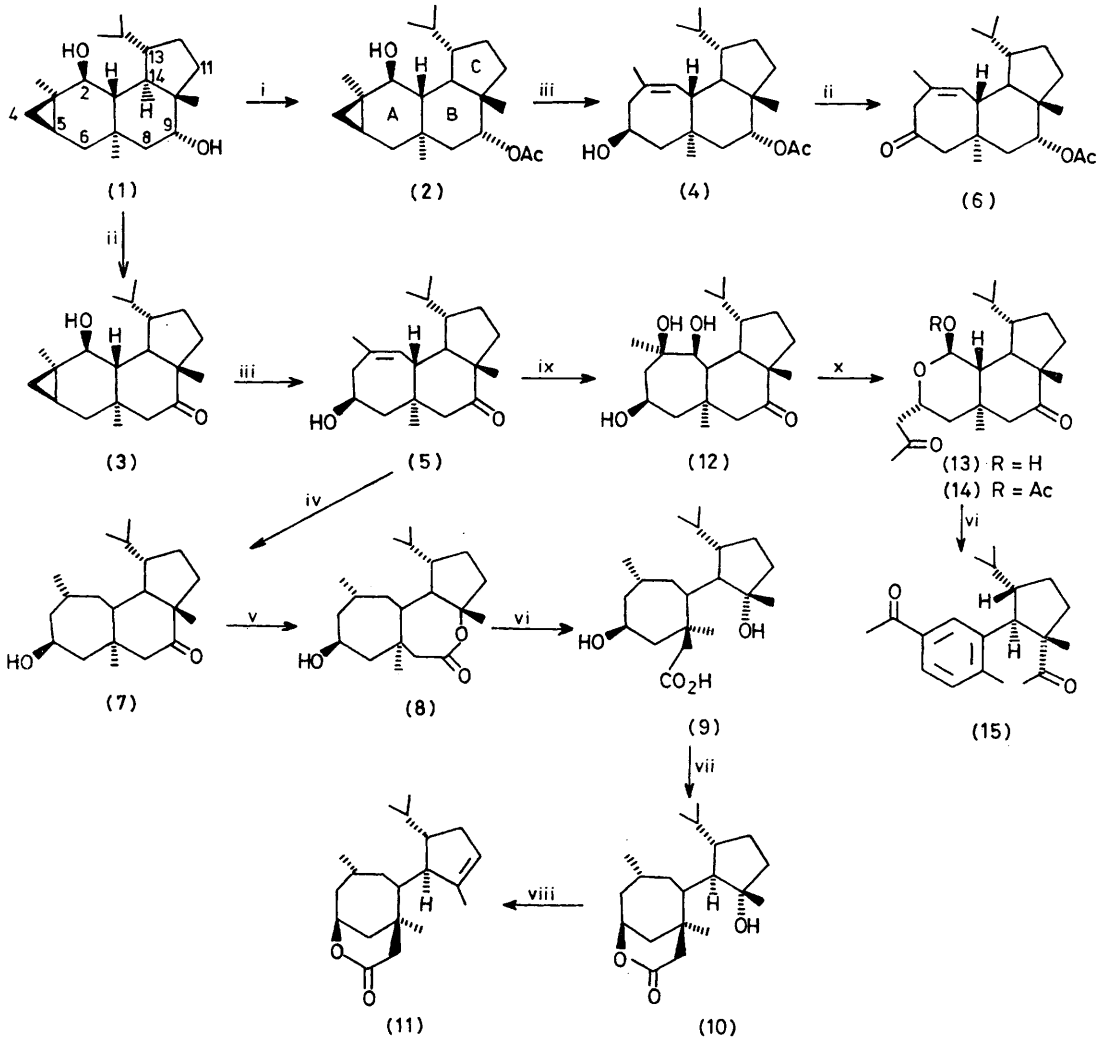
IN the course of our investigations on terpenoids from liverworts, a novel carbon skeletal diterpene diol, (−)-2,9-dihydroxyverrucosane, was isolated from an ethanolic extract of *Mylia verrucosa* Lindb. together with other diterpenoids having the same carbon skeleton, verrucosane. Structure (**1**) is proposed for the diol on the basis of the following experimental evidence.

Spectroscopic evidence showed that (**1**), $C_{20}H_{34}O_2$, m.p. 153—154 °C, $[\alpha]_D$ −72°, was a saturated tetracyclic diterpenoid containing a cyclopropane ring [ν 3060, 1012, and 1005 cm^{-1}; δ 0·1—0·7 (3H, complex m)], an isopropyl group [ν 1385, 1375, and 1170 cm^{-1}; δ 0·83 and 0·90 (each 3H, d, *J* 7 Hz)], 3 tertiary methyl groups [δ 0·77, 1·03, and 1·20 (each 3H, s)], and 2 secondary OH groups [ν 3525, 3400, and 1030 cm^{-1}; δ 3·45—3·80 (2H, complex m)]. This structure was supported by the off-resonance ^{13}C n.m.r. spectrum which showed 3 singlets (δ 23·4, 36·8, and 48·5 p.p.m.), 7 doublets (δ 25·2, 29·1, 40·3, 43·0, 46·3, 73·4, and 73·5 p.p.m.), 5 triplets (δ 18·3, 21·8, 32·9, 42·3, and 43·9 p.p.m.), and 5 quartets (δ 15·1, 19·1, 21·2, 22·2, and 23·4 p.p.m.).

The diol (**1**) gave the monoacetate (**2**), $C_{22}H_{36}O_3$, $[\alpha]_D$ −68° which contained an equatorial OH [δ 3·55 (1H, d, *J* 10 Hz)] and an axial acetoxy-group [δ 4·74 (1H, t, *J* 2·5 Hz)] along with the original cyclopropane, isopropyl, and 3 tertiary methyl groups.† Compound (**1**) also produced the hydroxy-ketone (**3**), $C_{20}H_{32}O_2$, m.p. 111—112 °C, $[\alpha]_D$ −151°, having an equatorial OH [δ 3·67 (1H, d, *J* 8·5 Hz)] and a six-membered ring ketone containing an adjacent active methylene besides the original groups. The spectral data of the two derivatives showed that (**1**) had the following two partial units: ⩾C–CH(OH)–CH and ⩾C–CH_2–CH(OH)–C⩽.

The monoacetate (**2**) and the hydroxy-ketone (**3**) were, respectively, converted into the unsaturated acetoxy-alcohol (**4**), $C_{22}H_{36}O_3$, and the unsaturated keto-alcohol (**5**), $C_{20}H_{32}O_2$, m.p. 133—135 °C, $[\alpha]_D$ −35°, in good yields. The spectral data of these products suggested the presence of a

† The ^1H n.m.r., i.r., and mass spectra of all new compounds (**1**)—(**15**) were consistent with the proposed structures.



Reagents: i, Ac_2O in pyridine; ii, CrO_3 in acetone; iii, 0·5 M H_2SO_4 in acetone; iv, H_2–PtO_2; v, *m*-$ClC_6H_4CO_3H$; vi, 5% NaOH in methanol; vii, Ac_2O; viii, $POCl_3$ in pyridine; ix, OsO_4 in benzene; x, $NaIO_4$.

trisubstituted double bond bearing a methyl group and a new secondary OH instead of the cyclopropane ring and the original secondary OH. Compound (**4**) was oxidized to the acetoxy–ketone (**6**), $C_{22}H_{34}O_3$, m.p. 110—111 °C, $[\alpha]_D$ −102°, which contained two newly formed active methylene groups (two AB-systems) and a trisubstituted double bond bearing a methyl group. Accordingly, (**6**) was deduced to be a seven-membered ring ketone including the partial structure, $\geqslant C\text{–}CH_2\text{–}CO\text{–}CH_2\text{–}C(Me)=CH\text{–}CH\leqslant$. The formation of compounds (**4**) and (**5**) could be reasonably explained in terms of homoallylic ring expansion of a cyclopropyl methanol unit in which, as shown by Gasie *et al.*,[1] the newly formed secondary OH is *cis* to the original secondary OH. Furthermore, the cyclopropane ring should have the same β-configuration as that of the C-1 methine proton because this proton was shielded so that its resonance was at δ *ca.* 0·9 by the anisotropic effect of the cyclopropane ring.[2] This was confirmed by a decoupling experiment between the C-1 and C-2 protons (δ 3·55, d, *J* 10 Hz) in the spectrum of the hydroxy-acetate (**2**).

The homoallylic alcohol (**5**) could be transformed to the dihydro-compound (**7**), $C_{20}H_{34}O_2$, m.p. 116·5—118 °C, the seven-membered ring lactone (**8**), $C_{20}H_{34}O_3$, m.p. 122·5—123 °C, and the acid (**9**), $C_{20}H_{36}O_4$, and then into the six-membered ring lactone (**10**), $C_{20}H_{34}O_3$. The formation of the lactone (**10**) showed that the junction between the A and B rings was *trans*, *i.e.* the tertiary C-7 methyl group had the α-configuration. From the hydroxy-lactone (**10**) the cyclopentene (**11**), $C_{20}H_{32}O_2$, with a trisubstituted double bond was obtained. Assuming the dehydration proceeds in the *trans*-direction, the B-C ring junction should be *trans*. The remaining C ring must consist of a cyclopentane ring bearing an isopropyl group whose presence was indicated by the doublet at 1380 cm^{-1} and an absorption at *ca.* 1170 cm^{-1} in the i.r. spectra of all derivatives.[3]

The homoallylic alcohol (**5**) was oxidized to the 1,2,4-triol (**12**), $C_{20}H_{34}O_4$, m.p. 127·5—129 °C, glycol fission of which gave directly the hemiacetal (**13**), $C_{20}H_{32}O_4$. When the acetate (**14**), $C_{22}H_{34}O_5$, derived from the hemiacetal (**13**), was kept for 3 h in 5% methanolic NaOH at room temperature,

the 3,4-disubstituted acetophenone (**15**), $C_{20}H_{28}O_2$, [λ(EtOH) 257·5 nm (ϵ 4600); ν 1700, 1680, and 1600 cm^{-1}; δ 0·77 (6H, d, *J* J Hz), 0·85, 2·06, 2·33, and 2·52 (each 3H, s), 3·83 (1H, d, *J* 8 Hz), 7·22 (1H, d, *J* 8 Hz), 7·67 (1H, dd, *J* 8 and 2 Hz) and 7·87 (1H, d, *J* 2 Hz)] was obtained in good yield. The size of the coupling (8 Hz) of the signal at δ 3·83 assigned to the benzyl methine proton indicates that the cyclopentane ring is in the envelope conformation with the C-13 and C-14 hydrogens *trans*-diaxial. This structure was supported by the ^{13}C n.m.r. spectrum: 6 × s (δ 212·1, 197·3, 143·2, 141·5, 135·0, and 59·1 p.p.m.), 6 × d (δ 130·6, 128·3, 126·1, 53·3, 48·6, and 31·2 p.p.m.), 2 × t (δ 38·2 and 27·1 p.p.m.), and 6 × q (δ 26·2, 25·7, 22·0, 21·5, 20·5, and 19·2 p.p.m.). The formation of the acetophenone derivative (**15**) from the acetylated hemiacetal (**14**) is presumed to take place *via* hydrolysis, aldol condensation, dehydration, and retro-Michael-type reaction, successively.

The stereostructure (**1**)‡ deduced contains a novel fused 3,6,6,5-tetracyclic ring system in the *cis–trans-anti–trans*-configuration.

We thank the Japanese Ministry of Education for financial support and the Japan Society for the Promotion of Science for supporting D. T. as a visiting investigator at Hiroshima University.

(*Received*, 7*th October* 1977; *Com.* 1123.)

‡ Recently the structure and absolute configuration of (**1**) were confirmed by *X*-ray analysis of its mono-*p*-bromobenzoate (Y. Kushi, H. Nozaki, A. Matsuo, M. Nakayama, S. Hayashi, D. Takaoka, and N. Kamijo, full paper in preparation.)

[1] M. Gasie, D. Whalen, B. Johnson, and S. Winstein, *J. Amer. Chem. Soc.*, 1967, **89**, 6382.
[2] S. Forsen and T. Norin, *Tetrahedron Letters*, 1964, 2845.
[3] L. J. Bellamy, 'The Infra-red Spectra of Complex Molecules,' Methuen, London and Wiley, New York, 1964); K. Nakanishi, 'Infra-red Spectra,' Nankodo, Tokyo, 1966.