

**X-Ray Crystal Structure of (+)-Vitrenal, a Sesquiterpenoid Plant-growth Inhibitor containing a Novel Carbon Skeleton isolated from the Liverwort *Lepidozia vitrea***

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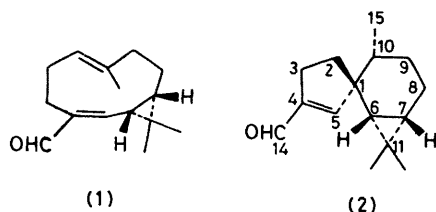
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*Summary* A sesquiterpenoid containing a novel carbon skeleton (+)-vitrenal, a plant-growth inhibitor, has been isolated from the liverwort *Lepidozia vitrea* and its structure and absolute configuration have been shown to be as in structure (2) on the basis of chemical and spectral evidence and X-ray analysis

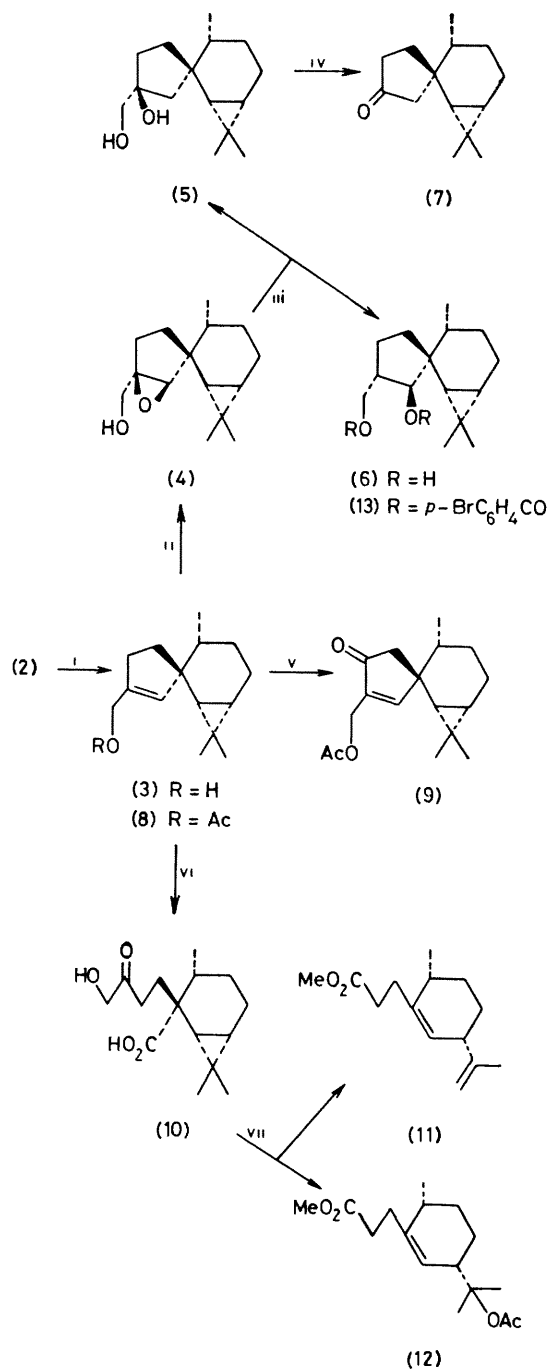
RECENTLY, we reported the isolation, from the liverwort *Lepidozia vitrea* Steph, and structural determination of (-)-isobicyclogermacrenal (1), a sesquiterpenoid which has an opposite absolute configuration to that of sesquiterpenoids from higher plants and displays plant-growth inhibiting properties<sup>1</sup> We have now isolated an additional plant-growth inhibitor, which we have named (+)-vitrenal,

and its structure and absolute configuration have been determined; it is also an enantiomeric type-sesquiterpenoid (2), with a novel carbon skeleton.† We report here the chemical and spectroscopic evidence and the result of X-ray crystal structure analysis for the proposed structure.



(+)-Vitrenal (2),  $C_{15}H_{22}O$ , oil,  $[\alpha]_D +107^\circ$ , was characterized as a tricycyclic sesquiterpenoid containing a cyclopropane ring [ $\delta$  0.7—0.8 (2H, m)], a secondary methyl group [ $\delta$  0.78 (3H, d,  $J$  5.5 Hz)], two tertiary methyl groups [ $\delta$  0.96 and 1.19 (each 3H, s)], and an  $\alpha,\beta$ -unsaturated aldehyde group conjugated with a trisubstituted double bond [ $\lambda$  242 nm ( $\epsilon$  13,200);  $\nu$  1680, 1613, and  $853\text{ cm}^{-1}$ ;  $\delta$  6.85 (1H, t,  $J$  1.5 Hz) and 9.75 (1H, s)].‡

On reduction with  $LiAlH_4$ , (2) gave the primary alcohol (3) whose off-resonance  $^{13}C$  n.m.r. spectrum showed 3 singlets, 4 doublets, 5 triplets, and 3 quartets. The epoxide (4) derived from (3) was converted by treatment with Li into the 1,2-diol (5) and the 1,3-diol (6), in a ratio of 1:3. The vicinal diol (5) was oxidized with  $NaIO_4$  to afford the ketone (7), showing a characteristic i.r. band at  $\nu$   $1740\text{ cm}^{-1}$  assigned to a 5-membered ketone. This chemical transformation (Scheme) suggested that the aldehyde group of (2) was attached to the cyclopentene ring. Since the  $^1H$  n.m.r. spectrum of the  $\alpha,\beta$ -unsaturated 5-membered ketone (9) [ $\lambda$  227 nm ( $\epsilon$  8860),  $\nu$   $1710\text{ cm}^{-1}$ ] produced by oxidation of the acetate (8) exhibited a pair of AB-type signals due to the methylene group adjacent to the carbonyl group at  $\delta$  2.39 and 2.75 ( $J$  18.5 Hz), one of the two quaternary carbon atoms was certainly located  $\beta$  to the carbonyl group as a spiro-carbon atom. The primary alcohol (3) was, furthermore, ozonolysed to a biscarbocyclic hydroxy-keto-acid (10) which, on treatment with  $Pb(OAc)_4$  and subsequent methylation, afforded two monocarbocyclic esters, (11) and (12) in a ratio of 1:1, undergoing oxidative cleavage of the 1,2-keto-alcohol moiety and decarboxylation accompanied by ring opening of the cyclopropane.<sup>2</sup> These products had an isopropenyl group [ $\nu$   $890\text{ cm}^{-1}$ ,  $\delta$  1.67 (3H, d,  $J$  1.0 Hz) and 4.64 (2H, brs)] and an acetoxy-isopropyl group [ $\nu$   $1735\text{ cm}^{-1}$ ,  $\delta$  1.38 (6H, s) and 1.94 (3H, s)], together with a trisubstituted double bond [ $\nu$   $864\text{ cm}^{-1}$ ,  $\delta$  5.20 (1H, br,  $w_{1/2}$  6.0 Hz) for (11);  $\nu$   $872\text{ cm}^{-1}$ ,  $\delta$  5.25 (1H, br,  $w_{1/2}$  5.0 Hz) for (12)], instead of the cyclopropane ring and two tertiary methyl groups. The full structure was, therefore, deduced to be (2) having the cyclopropane ring substituted with a geminal dimethyl group  $\alpha,\beta$  to the spiro-carbon on the 6-membered ring, as well as the spiro[4.5]decane system. However, the position of the secondary methyl group was suggested only by the biogenetic isoprene rule.<sup>3</sup>



SCHEME Reagents: i,  $LiAlH_4$  in ether; ii,  $m\text{-ClC}_6\text{H}_4\text{CO}_3\text{H}$  in  $\text{CHCl}_3$ ; iii, Li in  $\text{NH}_2\text{-(CH}_2\text{)}_2\text{-NH}_2$ ; iv,  $NaIO_4$ ; v,  $\text{CrO}_3$ -pyridine in  $\text{CH}_2\text{Cl}_2$ ; vi,  $\text{O}_3$  and  $\text{H}_2\text{O}_2$ ; vii,  $\text{Pb(OAc)}_4$  in benzene and  $\text{CH}_2\text{N}_2$

For confirmation of the structure and establishment of the absolute configuration, X-ray crystallographic analysis of the di-*p*-bromobenzoate (13) of the diol (6) was carried out.

† We propose the name vitrane for the new carbon skeleton and suggest the numbering shown in (2).

‡ All new compounds gave satisfactory combustion and/or mass spectrometric analysis and spectroscopic data consistent with the assigned structures.

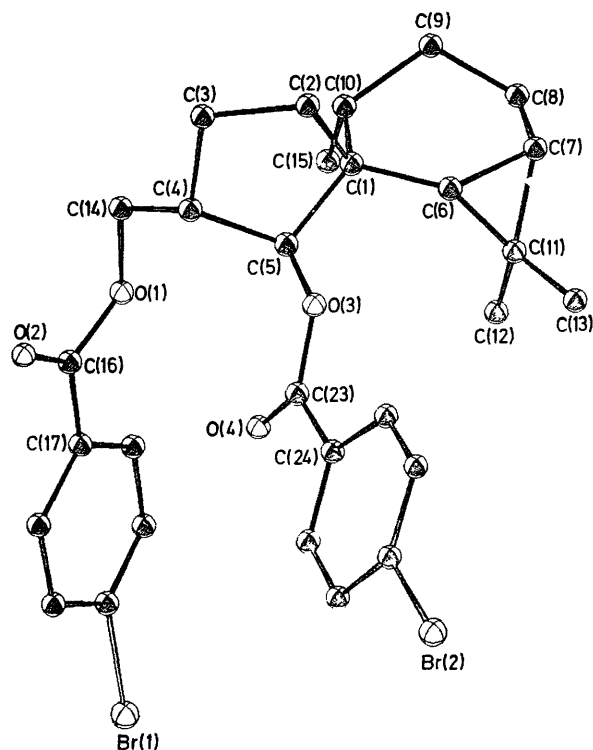


FIGURE A computer-generated perspective drawing of the di-*p*-bromobenzoate (**13**) derived from (+)-vitrenal (**2**). Hydrogen atoms have been omitted for clarity

Crystal data:  $C_{29}H_{34}Br_2O_4$ , orthorhombic, space group  $P2_12_12_1$ ,  $a = 9.568(3)$ ,  $b = 11.290(1)$ ,  $c = 24.819(11)$  Å,  $D_c = 1.50$  g cm $^{-3}$ ,  $Z = 4$ . The intensity data were

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

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<sup>2</sup> W Cocker, D P Hanna, and P V R Shannon, *J Chem Soc C*, 1968, 489

<sup>3</sup> L Ruzicka, *Experientia*, 1953, 9, 357

<sup>4</sup> W C Hamilton, *Acta Crystallogr*, 1965, 18, 502

<sup>5</sup> S Hayashi and A Matsuo, *Chemistry*, 1976, 31, 518 and references therein, A Matsuo, H Nozaki, M Nakayama, Y Kushi, S Hayashi, V Benešová, and V Herout, *J Chem Soc, Chem Commun*, 1976, 1006, A Matsuo and S Hayashi, *ibid*, 1977, 566, A Matsuo, S Uto, K Sakuda, Y Uchio, M Nakayama, and S Hayashi, *Chem Lett*, 1979, 73, A Matsuo, S Sato, M Nakayama, and S Hayashi, *J Chem Soc, Perkin Trans 1*, 1979, 2652, A Matsuo, K Atsumi, M Nakayama, S Hayashi, and K Kuriyama, *J Chem Soc, Chem Commun*, 1979, 1010

<sup>6</sup> R H Whittaker and P P Feeny, *Science*, 1971, 171, 757

collected on a four-circle diffractometer with graphite-monochromated Mo- $K_\alpha$  radiation. The positions of the two bromine atoms were determined from a Patterson synthesis and the subsequent electron density synthesis revealed the non-hydrogen atom skeleton, and the thirty-four hydrogen atoms were located using the difference electron density synthesis. The refinement by full-matrix least-squares, using anisotropic temperature factors, converged to a current  $R$  value of 0.073. At this stage, the anomalous scattering factor corrections for the bromine atoms were introduced into structure-factor calculations to establish the absolute configuration. For the configuration (**13**),  $R$  was 0.070 whereas for the inverted configuration it was 0.081.<sup>4</sup> Further full-matrix least-squares iterations reduced the  $R$  factor to 0.067 for 1170 reflections. The Figure shows a perspective drawing of the structure of the benzoate (**13**).<sup>5</sup> The sesquiterpenoid belongs to the enantiomeric series having the cyclopropane ring in the  $\alpha$ -orientation and the secondary methyl group *cis* to the cyclopropane.

Accordingly, the structure, including the absolute configuration, of (+)-vitrenal was determined as (**2**). This enantiomeric structure agrees with the result that most of the liverworts produce enantiomeric sesquiterpenoids.<sup>5</sup> (+)-Vitrenal (**2**) inhibits completely the growth of leaves and roots of rice seedlings at a concentration of 25 p.p.m. ( $1.1 \times 10^{-4}$  M) and the concentration for 50% growth inhibition ( $I_{50}$ ) is 18 p.p.m. It may be acting as allomone,<sup>6</sup> together with (-)-isobicyclogermacrene (**1**), in ecological systems.

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