

(-)-LEPIDOZENAL, A SESQUITERPENOID WITH A NOVEL *TRANS*-FUSED
BICYCLO[8.1.0]UNDECANE SYSTEM FROM THE LIVERWORT *LEPIDOZIA VITREA*

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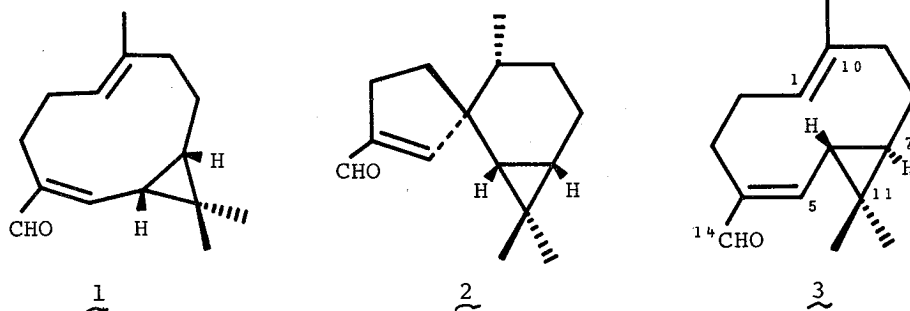
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A sesquiterpene aldehyde, (-)-lepidozenal, having a novel
trans-fused bicyclo[8.1.0]undecane carbon skeleton has been isolated
from the liverwort *Lepidozia vitrea*, and its structure and absolute
configuration have been shown to be (6*S*,7*R*)-lepidozal-1(10)*E*,4*E*-
dien-14-al, on the basis of the chemical and spectral evidence.

From the leafy liverwort *Lepidozia vitrea* Steph., we previously isolated two
sesquiterpene aldehydes, (-)-isobicyclogermacrenal (1) and (+)-vitrenal (2),
displaying plant-growth inhibiting properties and elucidated their structures
including the absolute configurations.^{1,2)} The stereostructures of these
sesquiterpenoids were enantiomeric type corresponding to the antipodes for normal
structures in higher plants. This result agrees with our finding that the
liverworts generally produce the enantiomeric sesquiterpenoids as the most
significant biochemical characteristic.³⁾ We now isolated the third sesquiterpene
aldehyde named (-)-lepidozenal, C₁₅H₂₂O, [α]_D -169°, from the methanol extract by
combination of column chromatography and preparative TLC together with two
enantiomeric sesquiterpene hydrocarbons, *ent*-bicyclogermacrene and *ent*-
aromadendrene. The structure including the absolute configuration has been shown
to be (6*S*,7*R*)-lepidozal-1(10)*E*,4*E*-dien-14-al (3) having a novel *trans*-fused
bicyclo[8.1.0]undecane system, lepidozane.⁴⁾ We report here the chemical and



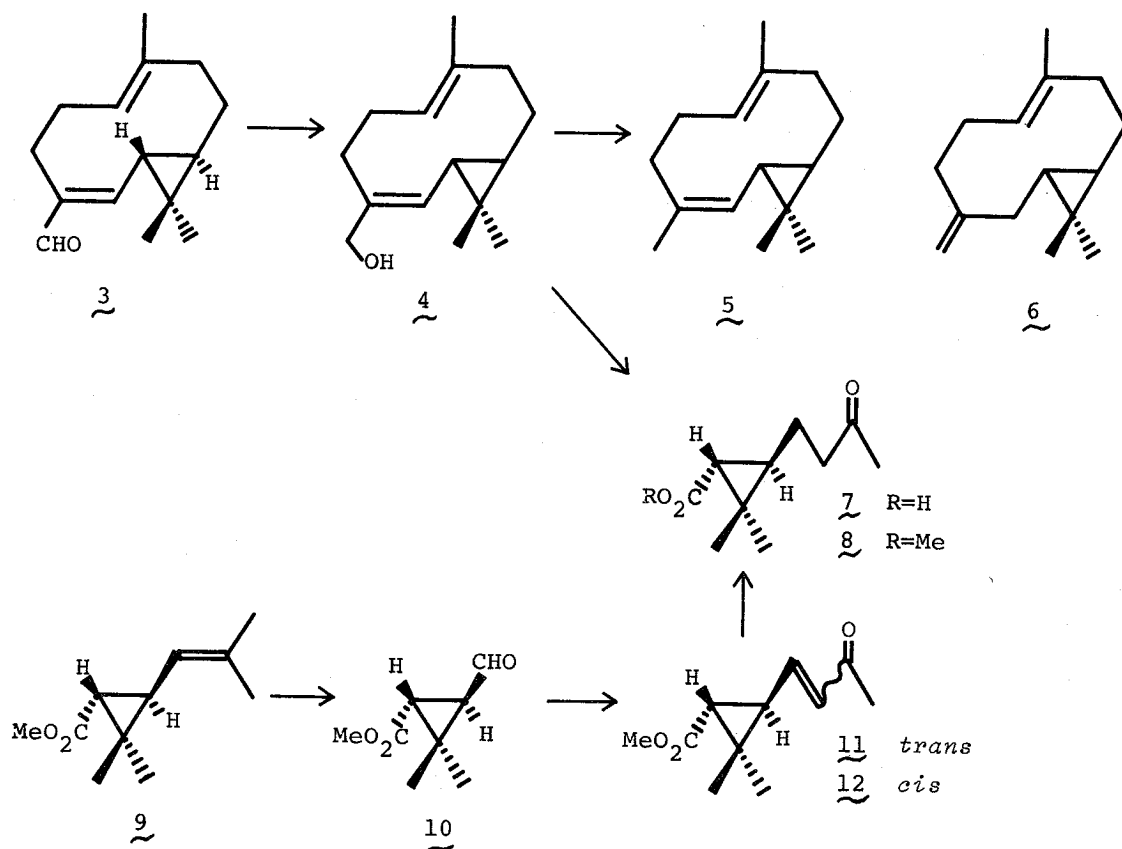
spectral evidence for the proposed structure.

(-)-Lepidozenal (3) was revealed by the spectroscopic properties as a bicyclic sesquiterpenoid containing a formyl group conjugated with a trisubstituted double bond [λ (EtOH) 265 nm (ϵ 14000); ν (CCl₄) 1685 and 1630 cm⁻¹; δ (CDCl₃) 6.33 (1H, d, J =10.0 Hz) and 9.30 (1H, s)] and another trisubstituted double bond with a methyl group [ν 870 cm⁻¹; δ 1.64 (3H, d, J =1.5 Hz) and 5.05 (1H, m)] as well as a *gem*-dimethyl cyclopropane ring [δ 0.4-1.0 (2H, complex) and 1.15 and 1.25 (each 3H, s)].⁵⁾ A strong resemblance of the spectra to those of (-)-isobicyclogermacrenal (1) suggested that 3 was a stereoisomer of 1 with respect to one of three geometries on the two double bonds and one cyclopropane ring existing in these molecules.

The aldehyde (3) was reduced with LiAlH₄ to afford an allylic primary alcohol (4), C₁₅H₂₄O, treatment of which with C₅H₅N-SO₃ followed by LiAlH₄ gave α -lepidozene (5), C₁₅H₂₄, along with β -lepidozene (6), C₁₅H₂₄, having an isomerized exocyclic double bond, in a ratio of 6 : 1. The major hydrocarbon showed the different spectra from not only those of isobicyclogermacrene but also those of bicyclogermacrene.^{6,7)} The geometries of two double bonds were clarified as 1,10-*trans* and 4,5-*cis* by the chemical shift of 10-methyl (δ 15.5) on ¹³C-NMR of the alcohol (4) and those of both 10-methyl (δ 15.5) and 4-methyl (δ 24.1) of the hydrocarbon (5).⁸⁾ The *trans* and *cis* orientations were also supported on the basis of NOE experiment of the original aldehyde (3): integrated intensity of the 5-H signal (δ 6.33) increased about 16% when the formyl proton (δ 9.30) was saturated by double irradiation. The saturation of 10-methyl (δ 1.64), however, caused no increase in the intensity of the 1-H signal (δ 5.05). From these results the structure of lepidozenal (3) should be a novel *trans*-fused bicyclo[8.1.0]undecane system. On the other hand, the alcohol (4) was submitted to ozonolysis to give a ketoacid (7), C₁₀H₁₆O₃, [α]_D -15.2°, which was then changed to a methyl ester

(8), $C_{11}H_{18}O_3$, $[\alpha]_D -22.8^\circ$. In the 1H -NMR spectrum of 8 added with $Eu(fod)_3$ (0.25 molar equivalent) the cyclopropane proton adjacent to the methoxycarbonyl group appeared clearly at δ 2.33 with coupling constant of 5.5 Hz which contrasted with the coupling constant (8.0 Hz) of the *cis*-ketoester derived from 1 and suggested a *trans*-orientation of the *cis*-dimethyl cyclopropane ring.⁹⁾ Both the ^{13}C -NMR spectra of the *trans*- and *cis*-ketoester were correlative to those of the methyl esters of *trans*- and *cis*-chrysanthemic acid, respectively.¹⁰⁾

For establishment of the absolute configuration, (-)-ketoacid (7) and (-)-ketoester (8) were directly compared with the corresponding compounds prepared from (+)-methyl *trans*-chrysanthemate (9): the ester (9), $C_{11}H_{18}O_2$, $[\alpha]_D +24.1^\circ$, which was obtained by methanolysis of (+)- β -allethrin,^{11,12)} was degraded by ozonolysis to an aldehyde (10), $C_8H_{12}O_3$, $[\alpha]_D +15.6^\circ$. It was then submitted to Wittig reaction to afford two kinds of ketone (11) and (12), $C_{11}H_{16}O_3$, containing *trans*- and *cis*-double bond, in a ratio of 7 : 1. These compounds were respectively hydrogenated to produce (-)-*trans*-ketoester (8), $C_{11}H_{18}O_3$, $[\alpha]_D -29.5^\circ$, which was, furthermore, hydrolyzed to (-)-*trans*-ketoacid (7), $C_{10}H_{16}O_3$, $[\alpha]_D -21.6^\circ$. The spectral data and the signs of optical rotations of both the ketoacid (7) and the



ketoester (8) derived from (-)-lepidozenal (3) were coincident, respectively, with those of the *trans*-ketoacid (7) and the *trans*-ketoester (8) prepared from (+)-methyl *trans*-chrysanthemate (9).

Thus, the structure of (-)-lepidozenal including the absolute configuration has been determined as (6*S*,7*R*)-lepidozal(10)*E*,4*E*-dien-14-al (3). This is the first example of the naturally occurring sesquiterpenoid having a *trans*-fused bicyclo[8.1.0]undecane system, although an example of diterpenoid containing the same *trans* system has been reported.¹³⁾ The aldehyde (3) and the corresponding alcohol derivative (4) inhibit the growth of rice seedlings at concentration of 200 and 65 PPM, respectively.

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- 4) We propose the name lepidozane for the new *trans*-fused carbon skeleton and the numbering shown in 3.
- 5) The ¹H-NMR, IR, and mass spectra of all new compounds 3-8 were consistent with the proposed structures.
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