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STRUCTURAL AND ABSOLUTE CONFIGURATIONAL STUDIES OF STRIATENE, STRIATOL AND β-MONOCYCLONEROLIDOL, THREE SESQUITERPENOIDS FROM THE LIVERWORT PTYCHANTHUS STRIATUS (LEHM. ET LINDEMB.) NEES

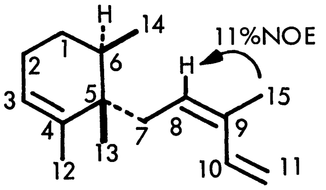
Reiji TAKEDA,* Reiko MORI, and Yoshio HIROSE
Suntory Institute for Bioorganic Research, Shimamoto-cho, Mishima-gun, Osaka 618

Three new sesquiterpenoids, striatene, striatol and β-monocyclonerolidol, were isolated from the liverwort Ptychanthus striatus (Lehm. et Lindemb.) Nees. Their structures have been established by spectroscopic analysis and chemical transformation.

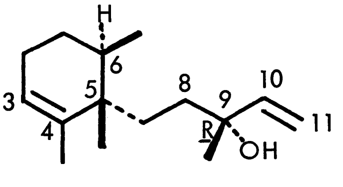
These compounds are interesting in terms of the evolution of the liverwort from algae.

We have recently reported$^{1)}$ the structure of "ptychanolide", a new type of sesquiterpenoid isolated from the liverwort Ptychanthus striatus, while Asakawa et al.$^{2)}$ have reported the characterization of mono- and sesquiterpene hydrocarbons, e.g., α-pinene, β-pinene, camphene, α-copaene and calamenene, from the same liverwort.

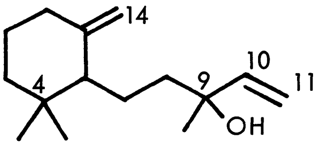
We report in the following the isolation and structural determination of three new sesquiterpenoids, striatene, striatol and β-monocyclonerolidol, which are interesting in terms of the evolution of the liverwort from algae. Striatene **1** (200 mg) and striatol **2** (70 mg) were isolated from the acetone extract of dry material (100 g) collected in Tokushima Prefecture in August 1979 by column chromatography on SiO_2 using hexane and CH_2Cl_2 followed by preparative GLC, while striatene **1** (200 mg) and β-monocyclonerolidol **3** (70 mg) were isolated from dry material (100 g) collected in Nara Prefecture in November 1979 by a similar procedure.



striatene **1**



striatol **2**



β-monocyclonerolidol **3**

The physical constants of striatene **1** and striatol **2** are as follows: Striatene **1**; $[\alpha]^{22}_{D}$ +72.7° (c = 1.19, $CHCl_3$), $C_{15}H_{24}$ (M^+, m/z 204), IR (film) 1640, 1600, 990, 810 cm^{-1}; UV $\lambda^{cyclohexane}_{max}$ 238 nm, ε = 24400 conjugated diene; ^1H-NMR (100 MHz, δ ppm, $CDCl_3$) 0.92 (3H, d, J = 6.5, 6-Me), 0.96 (3H, s, 5-Me), 1.69 (3H, br s, 4-Me), 1.88 (3H, br s, 9-Me), 2.18 (1H, dd, J = 6.0 and 16.0, 7-H_A), 2.49 (1H, dd, J = 8.0 and 16.0, 7-H_B), 5.25 (1H, dd, J = 1.6 and 10.5, 11-H_A), 5.28 (1H, dd, J = 1.6 and 17.3, 11-H_B), 5.34 (1H, m, 8-H), 5.56 (1H, t-like, 3-H) and 6.91 (1H, dd, J = 10.5 and 17.3, 10-H); ^{13}C-NMR (25.0 MHz, δ ppm, $CDCl_3$) four CH_3 (16.0, 19.2, 20.0 and 20.7), three CH_2 (25.3, 27.1 and 34.2), one CH (34.2), one C (40.7), one =CH_2 (113.2), three =CH (124.4, 128.1 and 134.0) and two =C (133.2 and 139.1). Striatol **2**; $[\alpha]^{25}_{D}$ + 49.5° (c = 1.2, $CHCl_3$); $C_{15}H_{26}O$ (M^+, m/z 222); IR (film) 3400, 1640, 990, 800 cm^{-1}; ^1H-NMR (100 MHz, δ ppm, $CDCl_3$) 0.87 (3H, d, J = 6.5, 6-Me), 0.88 (3H, s, 5-Me), 1.29 (3H, s, 9-Me), 1.59 (3H, br s, 4-Me), 5.09 (1H, dd, J = 1.6 and

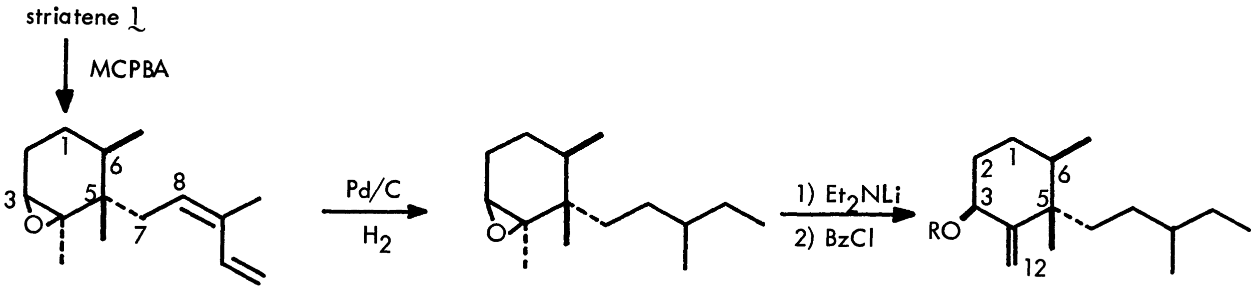
10.5, 11-H_A), 5.26 (1H, dd, J = 1.6 and 17.5, 11-H_B), 5.41 (1H, m, 3-H) and 5.92 (1H, dd, J = 10.5 and 17.5, 10-H); ^{13}C-NMR (25.0 MHz, δ ppm, $CDCl_3$) four CH_3 (15.7, 19.0, 21.0 and 27.6), four CH_2 (25.4, 27.0, 30.1 and 36.5), one CH (33.2), two C (40.0 and 73.1), one =CH_2 (111.4), two =CH (124.0 and 145.1) and one =C (139.3).

Dehydration of striatol 2 with $POCl_3$ in dry pyridine afforded two trienes, one of which was identified as striatene 1 by GLC, MS and IR. The above spectral data together with this result indicate that striatene and striatol have the same monocyclic carbon skeleton. The presence of a C_6 side chain was indicated by the mass spectrum of 1 which was marked by intense ions at m/z 123 (base peak, $M^+ - 81$) and m/z 81 originating by cleavage of the C-5/C-7 bond. Oxidation of 1 with MCPBA in CH_2Cl_2 at 0° gave two monoepoxides 4 and 5 which had a conjugated diene system (UV $\lambda_{max}^{cyclohexane}$ 238 nm, ϵ = 19500). The stereochemistries of oxirane rings in 4 and 5 were determined by ^1H-NMR using shift reagent Eu(fod)$_3$, *i.e.*, two protons of α-epoxide 5 at C-7 underwent a much larger shift than those of β-epoxide 4, thus showing that oxirane ring and side chain in 5 have a *cis* relation, while those in 4 have a *trans* relation. In the ^1H-NMR of one of the epoxides, 4, irradiation at δ 5.10 (8-H) collapsed the allylic methylene protons at 2.01 (7-H_A) and 2.45 (7-H_B) to AB type doublets and the olefinic methyl protons (9-Me) at 1.86 to a sharp peak. These results indicate that the C_6 side chain is 3-methyl-pent-1,3-diene.

In the ^1H-NMR of 2, the 6-H (*equatorial*, t, J = 6.1 Hz) and the 4-Me signals underwent a much larger shift than the 6-Me (*axial*) and the 5-Me signals upon addition of Eu(fod)$_3$. In the NOE experiment with 7 (described below) using 360 MHz NMR, a 2.3 % NOE was observed on 6-Me (*axial*) irradiation upon 5-Me.[3)] These results indicate that the 6-H and the hydroxy-containing side chain have a *cis* relation. The coupling pattern of the proton system in striatol 2 involving carbons 1, 2, 3, 4 and 6 was fully clarified by decoupling experiments with Eu(fod)$_3$. In the NOE experiment with striatene 1, an 11 % NOE was observed on 8-H upon irradiation of 9-Me, *i.e.*, geometry of the 8-ene is *Z*. These results lead to structures 1 and 2 for striatene and striatol, respectively.

The absolute configurations of 1 and 2 were determined in the following way. Hydrogenation of mono epoxide 4 with Pd/C gave tetrahydro compound 6 which was treated with diethylamine and n-BuLi[4)] in ether to give 7; this alcohol 7 was then reacted with *p*-Br-BzCl in pyridine to yield the corresponding monobenzoate 8. The conformation of this compound was determined to be as depicted in 8a by ^1H-NMR data including NOE experiments. The fact that 3-H is coupled with 2α- and 2β-H's with J = 5.3 and 10.9 Hz indicates that it is *axial*. An 11.0 % NOE is observed on 12-H_A upon irradiation of 5-Me, *i.e.*, it is *equatorial*. Harada *et al*.[5)] reported that the absolute configuration of cyclic allylic alcohols can be determined nonempirically by the CD exciton chirality method. Application of this method to benzoate 8, $\Delta\epsilon_{241}$ + 3.1, shows that the exocyclic double bond and the 3-OBz group constitute a positive chirality as shown in 8b. Thus, the absolute configuration of striatene is as shown in structure 1.

The configuration of the *tert*-OH group in 2 was determined by taking *R*-(-)-linalool 9 as the reference sample. Namely, it was found that the *p*-bromobenzoates of striatol and *R*-(-)-linalool both show negative Cotton effects at 252 nm (in MeOH), 2a $\Delta\epsilon$ - 0.4 and 9a $\Delta\epsilon$ - 0.5. This establishes the C-9 configuration in 2 to be *R*. Recently Gonnella *et al*.[6)] have shown that the benzoate method described above for cyclic compound is extensible to acyclic *sec*-allylic alcohols, namely, that the benzoate of acyclic allylic moiety 10 exhibits a positive CD. The present results including that of linalool show that the method is applicable to *tert*-OH system 11 as well (because the methyl group is smaller than other alkyl substituents).



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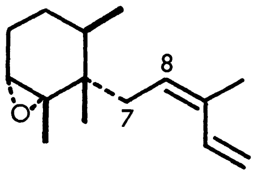
6

7 : R = H

8 : R = p-Br-Bz

+



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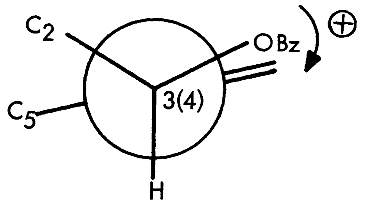
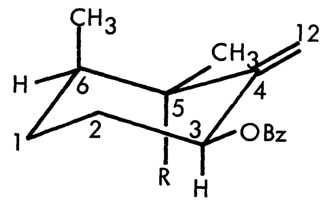
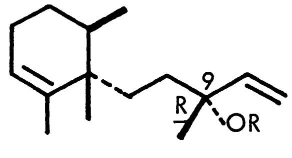


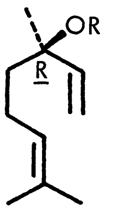
8b



8a

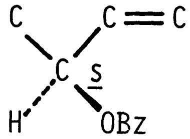


2a : R = p-Br-Bz



R-(-)-linalool 9 : R = H

9a : R = p-Br-Bz



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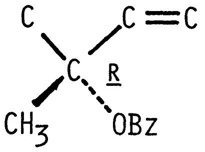
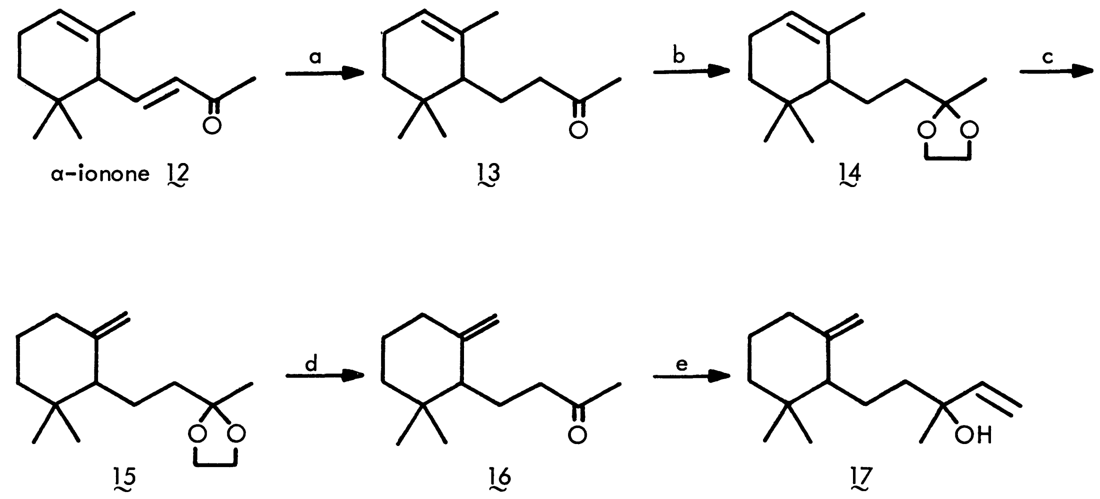


11

β-Monocyclonerolidol 3 exhibits the following constants: $[\alpha]_D^{25}$ + 3.2° (c = 0.66, $CHCl_3$); $C_{15}H_{26}O$ (M^+, m/z 222); IR (film) 3400, 1645, 990, 915, 890 cm^{-1}; ^1H-NMR (100 MHz, δ ppm, $CDCl_3$) 0.84 and 0.92 (3H, each, s, gem-dimethyl at C-4), 1.27 (3H, s, 9-Me), 4.53 (1H, br s, 14-H_A), 4.75 (1H, br s, 14-H_B), 5.02 (1H, dd, J = 1.6 and 10.5, 11-H_A), 5.18 (1H, dd, J = 1.6 and 17.5, 11-H_B) and 5.91 (1H, dd, J = 10.5 and 17.5, 10-H). ^{13}C-NMR (25.0 MHz, δ ppm, $CDCl_3$) three CH_3 (20.4, 26.4 and 27.7), five CH_2 (23.7, 28.5, 32.4, 36.2 and 41.1), one CH (54.5), two C (35.0 and 73.3), two =CH_2 (109.0 and 111.4), one =CH (145.4) and one =C (149.3).

From the above results we assumed that alcohol 3 has a monocyclonerolidol skeleton as shown in structure 3. This assumption was confirmed by partial synthesis from α-ionone in the following way. Hydrogenation of (±)-α-ionone 12 with Pd/C in 0.3 N KOH-EtOH gave the hydrogenated mixture from which dihydro-ionone 13 was separated by column chromatography on SiO_2. The reaction of 13 with ethylene glycol and p-TsOH gave ketal 14, which was irradiated in ether/10 % phenol with a 450W-Hg lamp[7] to afford a mixture of 15 and starting material 14; hydrolysis with p-TsOH in THF gave the ketones 16 and 13. The exocyclic isomer 16 which was separated by column chromatography on $AgNO_3$-SiO_2 was reacted with vinyl magnesium bromide in dry THF to give racemic alcohol 17. The NMR, IR and MS of compound 17 were identical with those of β-monocyclonerolidol 3.



a : H_2, Pd/C, 0.3N KOH-EtOH
b : Ethyleneglycol, p-TsOH
c : 10% Phenol/ether, hν(450W)
d : p-TsOH, THF
e : CH_2=CHMgBr, THF

On the basis of distribution of terpenoids, Asakawa and co-workers[8] have noted that liverwort are closely related to algae. The fact that the skeletal structures of 1~3 are identical with α- and β-snyderol,[9] microcionin,[10] *etc.*[11] which have been found in marine algae and in marine animals feeding on algae, supports the notion that liverworts have evolved from algae.

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