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SESQUITERPENOIDS FROM THE LIVERWORT *DICRANOLEJEUNEA YOSHINAGANA* (Hatt.) Mizut.

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A sesquiterpene alcohol with a new rearranged pinguisane carbon skeleton, which is named a neo-pinguisane type, has been isolated from the ether extract of the liverwort *Dicranolejeunea yoshinagana* (Hatt.) Mizut., together with two new pinguisane-type sesquiterpenoids and previously known deoxopinguisone and ptychanolide. Their structures were established by spectroscopic means.

KEY WORDS Hepaticae; Jungermanniales; Lejeuneaceae; *Dicranolejeunea yoshinagana*; neo-pinguisane; pinguisane

The stem-leafy liverwort, *Dicranolejeunea yoshinagana* (Hatt.) Mizut. belongs to the Jungermanniales and grows on deciduous plants or moist rock. In the genus of *Dicranolejeunea*, only one species is known in Asia and South America. The liverworts, including the Jungermanniales, are rich sources of terpenoids with a variety of carbon skeletons.1) Classification of the liverworts belonging to the Jungermanniales is morphologically extremely difficult, and thus a study of their chemical constituents is necessary. For this reason we have been investigating the chemosystematics of liverworts. Here we report on the isolation and structure elucidation of a novel sesquiterpene alcohol and two new pinguisane-type sesquiterpenoids from Japanese *D. yoshinagana,* a species which has not yet been investigated phytochemically.

Dicranolejeunea yoshinagana (Hatt.) Mizut. (31 g) was collected in July 1994 at Kami-gun, Beppu-valley, Kochi. A voucher specimen (# 94210) is deposited at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University.

The ether extract (680 mg) of *D. yoshinagana* was chromatographed repeatedly on silica gel and Sephadex LH-20 to give a novel sesquiterpene alcohol **1** (136.8 mg; 20.1% of the total extract) as the major constituent of this species, together with two new pinguisane-type sesquiterpenoids **2** (8.1 mg; 1.2 %) and **4** (6.8 mg; 1 %), deoxopinguisone (**5**)2) (7 mg; 1 %), ptychanolide (**6**)3) (9.7 mg; 1.4 %) and *ent*-(-)-bicyclogermacrene (**7**)4) (14.5 mg; 2.1 %; $[\alpha]_D$ -63° in acetone).

The EIMS of compound **1**, $[\alpha]_D$ -33.3° ($CHCl_3$; *c* 0.48), showed a molecular ion peak at *m/z* 222 and its HRMS indicated a molecular formula of $C_{15}H_{26}O$ (Calcd: 222.1984, Found: 222.1996). The ^{13}C NMR (Table 1) of **1** showed 15 carbons, while DEPT spectra located 25 of the 26 protons indicating the presence of an oxygenated nonprotonated carbon. All 26 protons were observed in the ^1H NMR spectrum, which contained an exchangeable hydroxyl proton. The IR spectrum of **1** contained a broad band at 3450 cm^{-1}, giving further support to the presence of a hydroxyl group. ^1H NMR data, including COSY analysis, were used to establish partial structures. Four methyl groups were indicated for **1**, with the signal at δ 1.22 (*s*, 3H) assigned to $-C(C\underline{H}_3)(OH)-$. The three vinyl protons observed at δ 5.13, 5.23 and 5.74 are characteristic of a $-CH=CH_2$ group, and the coupling of the vinyl proton at δ 5.74 with the doublet proton at δ 2.00 (*d*, *J*=10 Hz) indicated the presence of a $-CH-CH=CH_2$ unit in the structure of **1**. In addition to the above unsaturation, two rings must be

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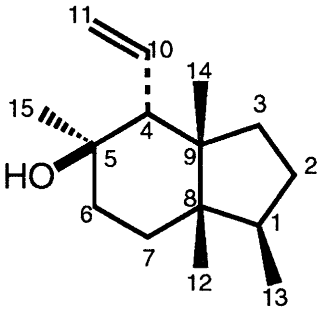
present. Four mutually coupled nonequivalent methylene protons were observed at δ 1.30, 1.44, 1.54 and 1.67, with their coupling constants suggesting a cyclohexane ring.

Table 1. NMR Spectral Data of **1**[a)]

	^{1}H	^{13}C [b)]	Long-range C/H correlations [c)] (^{13}C to ^{1}H)	NOE correlations [d)]
1	1.70 (*m*)	43.5	H-12, 13, 3β, 7α	
2	1.25 (*m*) 2.01 (*m*)	31.4	13	
3	1.29 (*m*) 1.92 (*ddd*, *J*=11, 11, 2)	32.7	14	
4	2.00 (*d*, *J*=10)	60.1	14, 15, 6α	
5		71.4	15, 7β, 6β, 4	
6	1.54 (*ddd*, *J*=14, 3, 3) 1.67 (*ddd*, *J*=14, 14, 3)	35.7	15	
7	1.30 (*ddd*, *J*=14, 3, 3) 1.44 (*ddd*, *J*=14, 14, 3)	37.7	12	
8		44.0	12, 14, 13, 2β, 7α, 6α, 4	
9		47.5	12, 14, 2β, α, 3α	
10	5.74 (*ddd*, *J*=17, 10, 10)	137.1		
11	5.13 (*dd*, *J*=17, 2) 5.23 (*dd*, *J*=10, 2)	119.2		
12	0.91 (3H, *s*)	17.0	7α	H-13, 14, 6β, 7β, 4
13	0.98 (3H, *d*, *J*=7)	20.2	2β	12, 14, 2β
14	0.80 (3H, *s*)	25.5	3α, 4	12, 13, 4, 2β, 3β
15	1.22 (3H, *s*)	25.3	6β	6α, 7α

[a)] Measured in chloroform-d_1, 600 MHz for ^{1}H, 100 MHz for ^{13}C. [b)] Assignments were confirmed by C/H-COSY spectrum. [c)] Confirmed by long-range C/H COSY spectrum. [d)] Observed by NOESY and difference NOE spectra.



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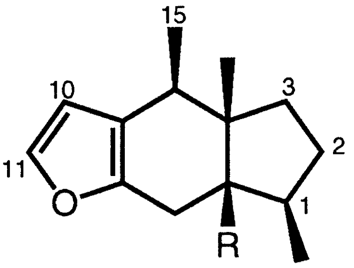
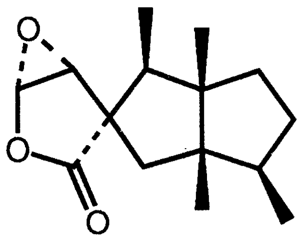


2 R=CHO
3 R=CH_2OH
4 R=CH_2OAc
5 R=CH_3



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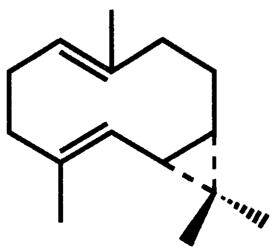

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The coupling of the methyl protons at δ 0.98 (*d*, *J*=7 Hz) with one [δ 1.70 (H-1)] of a set of five mutually coupled protons (δ 1.70, 2.01, 1.25, 1.29 and 1.92) indicated the presence of an isolated four carbon chain which includes the secondary methyl group. Partial structures were assembled using the C/H-COSY direct and long-range analyses (Table 1). The relative stereochemistry of **1** was established by NOE correlations (Table 1). Accordingly, consideration of the above spectral data led to the conclusion that the structure of **1**, which has a new rearranged pinguisane carbon skeleton, was determined as shown.

The ^{1}H NMR spectrum of compound **2**, $[\alpha]_D$ -49.7° ($CHCl_3$, *c* 0.64), showed a signal for a formyl proton at δ 9.52 (1H, *s*). The absorption bands of 2730 and 1730 cm^{-1} in its IR spectrum further supported the presence of an aldehyde. Reduction of **2** with $LiAlH_4$ afforded a primary alcohol **3** whose ^{1}H NMR spectrum indicated isolated methylene proton signals at δ 3.66 (*d*, *J*=12 Hz) and 3.81 (*d*, *J*=12 Hz). The mutually coupled proton signals in the ^{1}H NMR spectrum of **2** at δ 6.26 and 7.32 (each 1H, *d*, *J*=2 Hz) were characteristic of an α, β-substituted furan ring. The EIMS spectrum of **2** gave a molecular ion peak at *m/z* 232 and a base peak at *m/z* 108, which provided further evidence for this structure.[5] Methyl protons were observed for **2** at δ 0.79 (*s*), 0.89 (*d*, *J*=7 Hz) and 1.15 (*d*, *J*=7 Hz). Irradiation of the secondary methyl proton at δ 1.15 caused a broad quartet proton at δ 2.70 (*J*=7 Hz, H-4) to collapse to a sharp singlet signal, indicating the presence of an isolated -$CH(CH_3)$- unit. The coupling of the secondary methyl signal at δ 0.89 with one [δ 2.08 (H-1)] of the five mutually coupled protons [δ 2.08 (H-1), 1.36 (H-2), 1.96 (H-2), 2.22 (H-3β) and 1.55 (H-3)] indicated the presence of the same partial structure as **1**. The NOE correlations were observed by difference spectra as follows: between the tertiary methyl proton (3H-14) and the formyl proton, H-3β at δ 2.22 and a nonequivalent methylene proton at δ 2.51 (1H, *dd*, *J*=18, 3 Hz) which couples with a doublet signal at δ 2.80 (1H, *d*, *J*=18 Hz) and at long range couples with the H-4 proton with 3 Hz. The interpretation of the above spectral data is consistent with the structure of **2**, which possesses the pinguisane-type sesquiterpene skeleton.

The structure of compound **4**, $[\alpha]_D$ -70° ($CHCl_3$, *c* 0.3), was deduced by chemical correlation and its spectral data. The EIMS spectrum gave a molecular ion peak at *m/z* 276 and base peak at *m/z* 108. The IR and ^{1}H NMR spectral data of **4** closely resembled those of **2** except for lack of aldehyde proton and the presence of an acetyl group (1750 and 1250 cm^{-1}). Reduction of **4** with $LiAlH_4$ gave a primary alcohol whose ^{1}H NMR spectral data were identical with those of **3**. Accordingly, the structures of **2** and **4** were formulated as shown.

From the viewpoint of natural product chemistry, the biosynthesis of sesquiterpenoids **1-3** is of particular interest.

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