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New Sesqui- and Diterpenoids from the Japanese Liverwort *Jungermannia infusca* (MITT.) STEPH.

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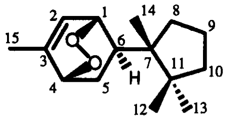
Two new peroxy cuparene-type sesquiterpenoids, a new 8,9-*seco*-labdane-type diterpenoid and previously known compounds, have been isolated from the diethyl ether extract of *Jungermannia infusca* and their structures elucidated from 2D NMR and/or X-ray crystallographic analysis.

Key words liverwort; *Jungermannia infusca*; Hepaticae; sesquiterpenoid; diterpenoid

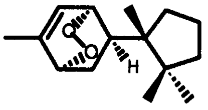
The liverwort (Hepaticae) *Jungermannia infusca* (MITT.) STEPH. belonging to the genus *Jungermannia* is morphologically complex, and therefore classification is difficult. The *Jungermannia* species contain mainly diterpenoids, such as clerodane-, labdane-, *ent*-kaurane-, pimarane- and trachylobane types.[1,2] As part of the search for novel compounds and biologically active substances from liverworts, we are continuing to study the chemical constituents of the Hepaticae.

J. infusca collected in different locations occasionally contain quite different diterpenoids as the main components. Recently, our group and Wu's group have independently reported on the isolation of bis(bibenzyl) aromatic compounds as the main components from Japanese[3,4] and Taiwanese[5] species, respectively. Therefore, to obtain new knowledge of the geographical chemical differences of *J. infusca*, we have reinvestigated the chemical constituents of the Japanese *J. infusca*.

The diethyl ether extract of *J. infusca* collected in Tochigi prefecture was subjected to column chromatography on silica gel and Sephadex LH-20 and preparative HPLC to yield two new peroxy cuparene-type, 1*R**,4*R**-peroxycupar-2-ene (**1**) and 1*S**,4*S**-peroxycupar-2-ene (**2**) and a new 8,9-*seco*-labdane-type diterpenoid **3**, together with the previously known cuparane-type sesquiterpenoids, (+)-cuprenenol[6] (**4**), rosulantol[6] (**5**), and labdane-type diterpenoid, (+)-labda-8(17),14-diene-9*R**,13*S**-diol[7] (**6**).



1



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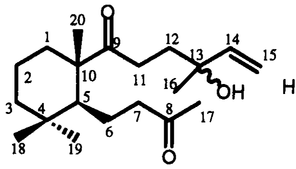

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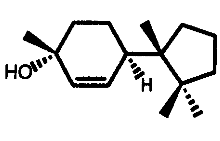

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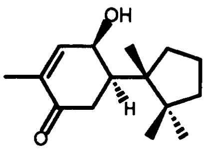

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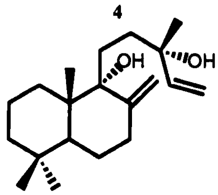

6

The molecular formula of **1** was $C_{15}H_{24}O_2$ (*m/z* 236.1786), indicating four degrees of unsaturation. The structure of **1**[8] was successively determined by analysis of spin–spin ^{1}H decoupling, and ^{13}C–^{1}H COSY and HMBC spectra. The stereochemistry was suggested by the difference NOE experiment observed between i) H-12$_{Me}$ and H-5β, H-13$_{Me}$, H-14$_{Me}$, ii) H-14$_{Me}$ and H-5β, H-12$_{Me}$, iii) H-13$_{Me}$ and H-10α, and iv) H-15$_{Me}$ and H-2, H-4. Furthermore, X-ray crystallographic analysis[9] confirmed the stereostructure of **1** to be as shown in Fig. 1. Thus the stereostructure of **1** was established to be 1*R**,4*R**-peroxycupar-2-ene, although the absolute structure remained to be clarified.

The molecular formula of **2**[10] was completely identical with that of **1**. The ^{1}H and ^{13}C NMR spectra of **2** were similar to those of **1**. Thus the structure of **2** was assumed to be the same peroxy cuparene-type sesquiterpenoid as **1**. To determine the structure, detailed analyses of ^{13}C–^{1}H COSY and HMBC spectra were carried out. The stereochemistry of **2** was supported by the NOESY spectrum in which NOEs were observed between i) H-12$_{Me}$ and H-5β, H-13$_{Me}$, H-14$_{Me}$, ii) H-13$_{Me}$ and H-5α, H-6, H-8α, H-12$_{Me}$, iii) H-14$_{Me}$ and H-1, H-2, H-5β, H-10β, H-8β, H-12$_{Me}$, and iv) H-6 and H-5α, H-8α, H-13$_{Me}$. Thus the structure of **2** was determined to be the 1,4-epimer of **1**.

The IR spectrum of compound **3**[11] showed the presence of hydroxyl and carbonyl groups and the EI-MS spectrum showed *m/z* 304 $[M-H_2O]^+$. The ^{1}H- and ^{13}C-NMR spectra exhibited the presence of four tertiary methyls, a methyl ketone, terminal-vinyl, tertiary alcohol, and

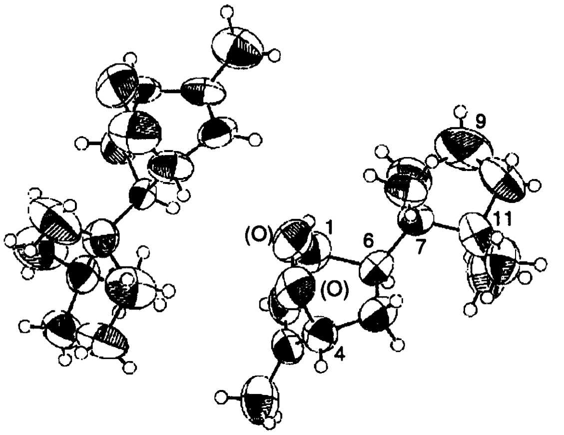

Fig. 1. ORTEP Drawing of **1**

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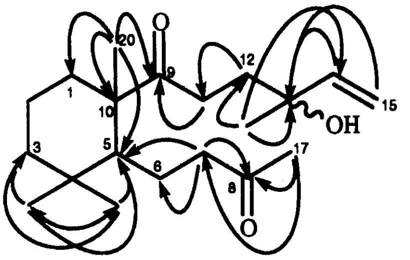

Fig. 2. Correlations Observed in the HMBC Spectrum of 3

ketones. These spectral data suggested that **3** is a monocyclic diterpenoid. Furthermore, detailed analysis of ^{1}H–^{1}H COSY, HSQC, and HMBC spectra clarified that compound **3** is a 8,9-*seco*-labdane-type diterpenoid, as shown in Fig. 2. The stereochemistry of **3** was determined by the NOESY spectrum observed between i) H-20$_{\mathrm{Me}}$ and H-18$_{\mathrm{Me}}$, H-3, H-11, ii) H-1 and H-11, H-18$_{\mathrm{Me}}$, H-6, iii) H-19$_{\mathrm{Me}}$ and H-5, and iv) H-6 and H-18$_{\mathrm{Me}}$, H-19$_{\mathrm{Me}}$. Thus the whole structure was established as shown in **3**.

The chemical constituents of *J. infusca* have already been studied and it was reported that *ent*-kaurane-type, clerodane- and labdane-type diterpenoids, and bis(bibenzyl) are the main components.[1,2] The present *J. infusca* is chemically quite different from the same species collected in different locations, since it produces mainly cuparene-type sesqui- and 8,9-*seco*-labdane-type diterpenoids.

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8) mp 77—78°C; $[\alpha]_D^{23}$ +28.9° (*c* 5.33, $CHCl_3$); HRMS *m*/*z*: 236.1786 $[M]^+$ $C_{15}H_{24}O_2$ requires 236.1777 ; IR: 1470, 1440, 1380, 1370, 920 cm^{-1}; δ_H ($CDCl_3$) 4.47 (1H, d, *J*=6.3 Hz, H-1), 6.37 (1H, dt, *J*=6.4, 2.0 Hz, H-2), 4.41 (1H, br s, H-4), 1.54 (1H, ddd, *J*=12.2, 11.2, 2.5 Hz, H-5α), 2.13 (1H, ddd, *J*=12.2, 5.4, 3.4 Hz, H-5β), 1.58 (1H, m, H-6), 1.60—1.70 (4H, m, H-8 and 9), 1.35 (1H, m, H-10α), 1.78 (1H, m, H-10β), 0.98 (3H, s, H-12), 0.82 (3H, s, H-13), 1.16 (3H, s, H-14), 1.95 (3H, d, *J*=2.0 Hz, H-15); δ_C ($CDCl_3$) 75.7 (C-1), 127.4 (C-2), 139.4 (C-3), 75.3 (C-4), 23.3 (C-5), 41.1 (C-6), 47.2 (C-7), 39.2 (C-8), 19.3 (C-9), 40.8 (C-10), 44.5 (C-11), 24.6 (C-12), 25.4 (C-13), 17.7 (C-14), 18.7 (C-15).

9) Recrystallized from *n*-pentane as a single crystal. Crystal data for **1**: orthorhombic, $a=11.461(5)$, $b=24.08(1)$, $c=10.191(6)$ Å, $V=2812.199951(2)$ Å^3, $Z=8$, space group $P2_12_12_1$, $Dx=1.114$ Mg m^{-3}, Cu-Kα radiation, $\lambda=1.54178$ Å, $\mu=5.302$ mm^{-1}. Diffraction measurements were made on a Mac Sciences MXC 18. The structure was solved by direct methods using CRYSTAN SIR92 and refined by full matrix least-squares. Final $R=0.085$, $Rw=0.104$, $S=2.575$.

10) $[\alpha]_D^{19}$ +136.2° (*c* 2.46, $CHCl_3$); HRMS *m*/*z*: 236.1770 $[M]^+$ $C_{15}H_{24}O_2$ requires 236.1776; IR: 1460, 1380, 930 cm^{-1}; δ_H ($CDCl_3$) 4.44 (1H, ddd, *J*=6.3, 2.5, 1.6 Hz, H-1), 6.20 (1H, d quit., *J*=6.3, 1.9 Hz, H-2), 4.46 (1H, m, H-4), 2.31 (1H, ddd, *J*=13.7, 9.1, 4.9 Hz, H-5α), 1.35 (1H, m, H-5β), 2.50 (1H, ddd, *J*=9.1, 6.9, 2.7 Hz, H-6), 1.82 (1H, like br q, H-8α), 1.49 (1H, ddd, *J*=12.1, 9.1, 3.0 Hz, H-8β), 1.58, 1.64 (each 1H, m, H-9), 1.36 (1H, m, H-10α), 1.67 (1H, m, H-10β), 0.86 (3H, s, H-12), 0.99 (3H, s, H-13), 0.60 (3H, s, H-14), 1.94 (3H, d, *J*=1.6 Hz, H-15); δ_C ($CDCl_3$) 74.6 (C-1), 124.8 (C-2), 139.8 (C-3), 76.2 (C-4), 27.1 (C-5), 41.5 (C-6), 45.7 (C-7), 39.1 (C-8), 19.2 (C-9), 40.6 (C-10), 44.4 (C-11), 24.6 (C-12), 25.4 (C-13), 19.0 (C-14), 18.3 (C-15).

11) $[\alpha]_D^{22}$ −3.2° (*c* 3.00, $CHCl_3$); HRMS *m*/*z*: 304.2420 $[M-H_2O]^+$ $C_{20}H_{32}O_2$ requires 304.2403; IR: 3480, 1700, 1365 cm^{-1}; δ_H ($CDCl_3$) 1.39 (1H, m, H-1), 1.47 (1H, m, H-1), 1.49 (1H, m, H-2), 1.56 (1H, like tt, H-2), 1.16—1.23 (2H, m, H-3 , 6), 1.41 (1H, m, H-3), 1.72 (1H, t, *J*=4.7 Hz, H-5), 1.61 (1H, m, H-6), 2.39 (1H, tt, *J*=17.5, 5.5 Hz, H-7), 2.44 (1H, tt, *J*=17.3, 5.5 Hz, H-7), 2.56 (1H, ddd, *J*=18.1, 7.7, 6.9 Hz, H-11), 2.61 (1H, ddd, *J*=18.1, 7.7, 6.3 Hz, H-11), 1.73 (1H, ddd, *J*=14.6, 7.7, 6.3 Hz, H-12), 1.82 (1H, ddd, *J*=14.6, 8.0, 6.9 Hz, H-12), 5.83 (1H, dd, *J*=17.3, 10.7 Hz, H-14), 5.07 (1H, dd, *J*=10.7, 1.4 Hz, H-15), 5.23 (1H, dd, *J*=17.3, 1.4 Hz, H-15), 1.29 (3H, s, H-16), 2.09 (3H, s, H-17), 0.92 (3H, s, H-18), 0.91 (3H, s, H-19), 1.22 (3H, s, H-20); δ_C ($CDCl_3$) 37.2 (C-1), 18.2 (C-2), 41.1 (C-3), 34.3 (C-4), 47.7 (C-5), 22.2 (C-6), 45.6 (C-7), 209.2 (C-8), 218.2 (C-9), 53.2 (C-10), 32.5 (C-11), 35.7 (C-12), 72.6 (C-13), 144.4 (C-14), 112.2 (C-15), 28.8 (C-16), 29.9 (C-17), 22.5 (C-18), 33.4 (C-19), 17.3 (C-20).