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# NEW HIGHLY OXYGENATED 6,7-SECO-KAURANE- AND BIS-KAURANE-TYPE DITERPENOIDS FROM THE LIVERWORT *JUNGERMANNIA EXSERTIFOLIA* STEPH. SSP. *CORDIFOLIA* (DUM.) VANA

Fumihiro NAGASHIMA, Hironao TANAKA, Shigeru TAKAOKA, and Yoshinori ASAKAWA,*
Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770, Japan

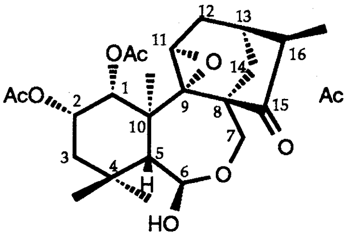
Two new 6,7-seco-kaurane-type diterpenoids, secoexsertifolins A (**1**) and B (**2**), and a new bis-kaurane-type diterpenoid, exsertifolin A (**3**), have been isolated and their structures determined by extensive spectroscopic and X-ray crystallographic analysis.

**KEYWORDS** *Jungermannia exsertifolia* ssp. *cordifolia*; liverwort; secoexsertifolin A; secoexsertifolin B; exsertifolin A; bis-kaurane

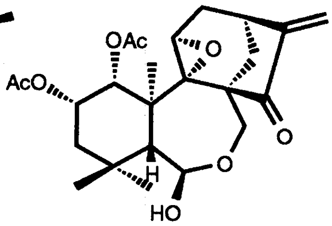
The liverwort *Jungermannia* species are rich sources of diterpenoids belonging to the pimarane, clerodane and kaurane classes [1]. *J. exsertifolia* ssp. *cordifolia* produces trachylobane-type diterpenoid [2]. As part of a chemosystematic study and search for biologically active substances, we have reinvestigated French *J. exsertifolia* ssp. *cordifolia* and isolated two new 6,7-seco-kaurane-type diterpenoids **1** and **2**, and bis-kaurane-type diterpenoid **3**, and established their structures on the basis of spectral evidence and X-ray crystallographic analysis. The ether extract of *J. exsertifolia* ssp. *cordifolia* (4.2 g)was chromatographed on silica gel, Sephadex LH-20 and preparative HPLC to give two new 6,7-seco-kaurane-type diterpenoids, secoexsertifolins A (**1**, 26 mg) and B (**2**, 10 mg), and a new bis-kaurane-type diterpenoid, exsertifolin A (**3**, 20 mg), and a previously known, *ent*-11α-hydroxy-16-kauren-15-one [3,4] (**4**, 50 mg).

Compound **1**[5] has the molecular formula $C_{24}H_{34}O_8$ (anal. 450.2261) by the high-resolution mass spectrum (HRMS). The $^{13}C$ NMR and IR spectra showed the presence of a hydroxyl group (3450 $cm^{-1}$), and a ketone (δ216.8 *s*) and two acetoxyl groups (1735, 1250 $cm^{-1}$ ; δ 169.1 *s*, 170.6 *s*, 20.8 *q*, 20.9 *q*). The $^1H$ NMR spectrum contained the signals of a secondary methyl, three tertiary methyls, two acetoxyl methyls, two methine protons (δ 4.87 *dd*, *J*=4.9, 2.0 Hz, 5.04 *ddd*, *J*=13.2, 4.9, 2.4 Hz) bearing acetoxyl group, a methine proton (δ 5.24 *dd*, *J*=9.3, 2.9 Hz) with hydroxyl group and an isolated methylene proton (δ 3.17, 4.69 each *d*, *J*=13.2 Hz). The $^{13}C$ NMR spectrum also showed the presence of six methyls, three methylenes, three methins, three quaternary carbons and two methine carbons (δ 66.7, 75.7) bearing acetoxyl group and also showed a hemiacetal carbon (δ 96.3), a methylene (δ 61.8), a methin (δ 50.3) and a quaternary carbon (δ 65.9) bearing an oxygen atom. The above spectral data and 2D-NMR ($^1H$-$^1H$, $^{13}C$-$^1H$ COSYs and the HMBC spectrum) experiments suggested that **1** might be 6,7-seco-kaurane-type diterpenoid with $C_9$-$C_{11}$ epoxide. This was confirmed by X-ray crystallographic analysis [6] (Fig. 1). The structure of secoexsertifolin B [7] was also established to be **2** by the formation of **1** on the hydrogenation of **2**.

FAB-mass spectrum of **3** [8] showed *m/z* 773 $[M^+ + Na]^+$. The $^{13}C$ NMR and IR spectra showed the presence of a hydroxyl (3500 $cm^{-1}$), two ketones (δ 209.5, 217.2 each *s*) and two acetoxyl groups (1740, 1250 $cm^{-1}$; δ 20.9 (x2) *q*, 169.1, 170.4 each *s*). The signals of $^1H$ and $^{13}C$ NMR closely resembled those of **1** and **4** [3,4]. Moreover, the $^{13}C$-$^1H$ COSY and HMBC spectra suggested that **3** might be a bis-kaurene-type diterpenoid having $C_7$ - $C_{11'}$ ether linkage between compounds **1** and **4**. This assumption was clarified by X-ray crystallographic analysis 9) as shown in Fig. 2. Thus, the structure of exsertifolin A was established to be **3** with bis-kaurene-type diterpenoid.



**1**



**2**

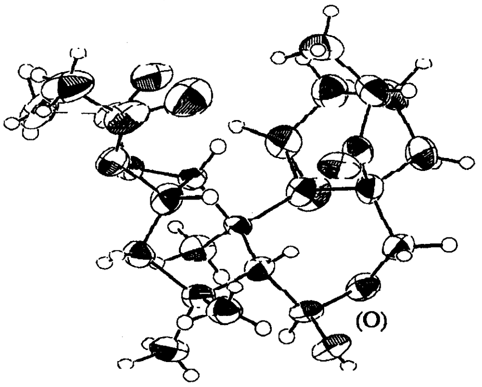
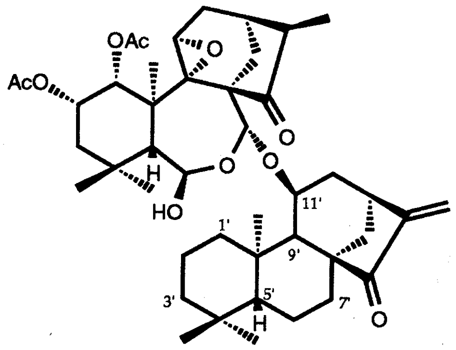
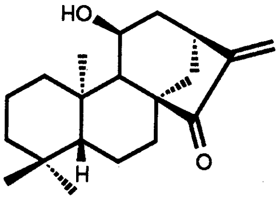


Fig. 1 ORTEP Drawing of **1**

Previously, we reported *J. exsertifolia* ssp. *cordifolia* which biosynthesizes trachylobane-type diterpenoid 2). However, the present species does not contain the trachylobane. Thus, there are at least two chemotypes of *J. exsertifolia* ssp. *cordifolia*. This is the first report of the isolation of the 6,7-seco-kaurane-type diterpenoids with $C_9$ - $C_{11}$ epoxide from nature and the third report of the isolation of the bis-kaurane-type diterpenoid from the liverwort 10,11). The absolute configurations of **1** - **3** remain to be clarified.



**3**



**4**

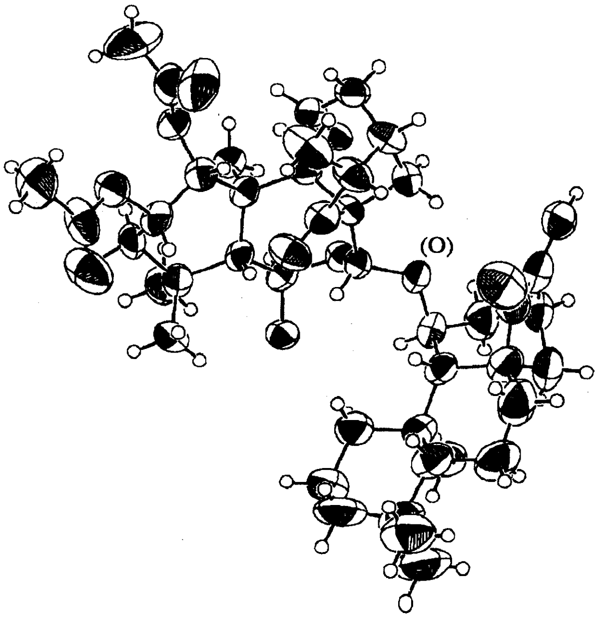


Fig. 2 ORTEP Drawing of **3**

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5) mp 218-219°C; $[\alpha]_D^{20}$ -43.7° (c 1.95, $CHCl_3$); HRMS; *m/z* 450.2261 $C_{24}H_{34}O_8$ requires 450.2254 ; CD (MeOH) $\Delta\varepsilon$ : +1.86 (290) (positive maximum) ; IR; 3450, 1735, 1250 cm$^{-1}$; $\delta_H$ ($CDCl_3$) 4.87(1H, *dd*, *J*=4.9, 2.0 Hz, H-1), 5.04(1H, *ddd*, *J*=13.2, 4.9, 2.4 Hz, H-2), 1.25(1H, *dt*, *J*=12.7, 2.4 Hz, H-3), 1.86(1H, *t*, *J*=12.2 Hz, H-3), 2.78(1H, *d*, *J*=9.8 Hz, H-5), 5.24(1H, *dd*, *J*=9.3, 2.9 Hz, H-6), 3.17(1H, *d*, *J*=13.2 Hz, H-7), 4.69(1H, *d*, *J*=13.2 Hz, H-7), 2.64(1H, *br s*, H-11), 1.93(2H, *m*, H-12), 2.17(1H, *br q*, H-13), 1.37(1H, *ddd*, *J*=12.2, 4.9, 1.5 Hz, H-14), 2.54(1H, *d*, *J*=12.2 Hz, H-14), 2.34(1H, *quit.*, *J*=7.3 Hz, H-16), 2.06(3H, *s*, -OAc), 1.92(3H, *s*, OAc), 1.32(3H, *d*, *J*=7.3 Hz, H-17), 1.41(3H, *s*, H-18), 1.13(3H, *s*, H-19), 0.88(3H, *s*, H-20) ; $\delta_C$ ($CDCl_3$) 75.7(C-1), 66.7(C-2), 38.5(C-3), 33.0(C-4), 44.1(C-5), 96.3(C-6), 61.8(C-7), 56.2 (C-8), 65.9(C-9), 46.1(C-10), 50.3(C-11), 23.3(C-12), 31.1(C-13), 39.4(C-14), 216.8(C-15), 47.7(C-16), 11.2(C-17), 32.8(C-18), 25.4(C-19), 15.5(C-20), 20.8, 20.9, 169.1, 170.6(OAc).

6) Recrystallized from *n*-hexane as single crystal. Crystal data for **1**; orthorhombic, a=12.856(2), b=17.531(14), c=10.173(2) Å, space group $P2_12_12_1$, Dcalc=1.30 Cu-K$\alpha$ radiation, $\lambda$=1.54178, $\mu$=7.15m$^{-1}$. Diffraction measurements were made on a Mac Sciences MXC 18. The structure was solved by direct methods using MONTECALRO and refined by full-matrix least-squares. Final R=0.051, $R_W$=0.072, S=3.03.

7) mp 217-219°C; $[\alpha]_D^{20}$ -25.8° (c 1.00, $CHCl_3$); HRMS; *m/z* 448.2098, $C_{24}H_{32}O_8$ requires 448.2097; CD (MeOH) $\Delta\varepsilon$ : +0.42 (390) (positive maximum) ; IR; 3450, 1740, 1250cm$^{-1}$; $\delta_H$ ($CDCl_3$) 4.96(1H,*d*, *J*=2.0 Hz, H-1), 4.93(1H, *m*, H-2), 1.26(1H, *br d*, H-3), 1.82-1.93(2H, *m*, H-3 and 12), 2.64(1H, *d*, *J*=9.8 Hz, H-5), 5.25(1H, *dd*, *J*=9.8, 2.9 Hz, H-6), 3.18(1H, *d*, *J*=13.2 Hz, H-7), 4.80(1H, *d*, *J*=13.2 Hz, H-7), 2.75(1H, *d*, *J*=4.9 Hz, H-11), 2.22(1H, *dd*, *J*=15.1, 5.4 Hz, H-12), 2.71(1H, *br t*, *J*=5.4 Hz, H-13), 1.42(1H, *m*, H-14), 2.39(1H, *d*, *J*=12.2 Hz, H-14), 5.57(1H, *s*, H-17), 6.34(1H, *s*, H-17), 1.41(3H, *s*, H-18), 1.14(3H, *s*, H-19), 0.89(3H, *s*, H-20), 1.90, 2.03(each 3H, *s*, OAc), 2.45(1H, *d*, *J*=2.9 Hz, OH); $\delta_C$ ($CDCl_3$) 74.6(C-1), 66.8(C-2), 38.7(C-3), 33.0(C-4), 44.3(C-5), 96.1(C-6), 60.7(C-7), 56.5(C-8), 67.1(C-9), 46.3(C-10), 50.5(C-11), 31.1(C-12), 32.8(C-13), 37.5(C-14), 202.8(C-15), 147.8(C-16), 121.5(C-17), 32.9(C-18), 25.3(C-19), 14.8(C-20), 20.8, 20.9, 169.2, 170.3 ( OAc).

8) Recrystallized from *n*-hexane as single crystal. Crystal data for **3**; monoclinic, a=16.411(5), b=10.500(4), c=14.292(5) Å, $\beta$=112.69 (2) °, space group $P2_1$, Dcalc=1.10, Cu-K$\alpha$ radiation, $\lambda$=1.54178, $\mu$=5.874cm$^{-1}$. Diffraction measurements were made on a Mac Sciences MXC 18. The structure was solved by direct methods using SHELXS 86 and refined by blockmatrix least-squares. Final R=0.1170, $R_W$=0.1104.

9) mp 198-200°C; $[\alpha]_D^{20}$ -67.6° (c 1.69, $CHCl_3$); FAB-MS; *m/z* 773 $[M^++Na]^+$; CD (MeOH) $\Delta\varepsilon$ : -0.08 (360), -0.13 (330), +1.70 (295), -2.30 (245) ; IR; 3500, 1740, 1250cm$^{-1}$; $\delta_H$ ($CDCl_3$) 4.86(1H, *br d*, H-1), 5.02(1H, *br d*, H-2), 5.23(1H, *dd*, *J*=9.8, 3.4 Hz, H-6), 5.44(1H, *s*, H-7), 2.54(1H, *m*, H-11), 2.24(1H, *m*, H-13), 1.28(3H, *d*, *J*=7.3 Hz, H-17), 1.35(3H, *s*, H-18), 1.10(3H, s, H-19), 0.84(3H, *s*, H-20), 1.91, 2.03(each 3H, s, OAc), 2.78(1H, *d*, *J*=3.4 Hz, OH), 2.16(1H, *br d*, H-1'), 3.89(1H, *br s*, H-11'), 2.01(2H, *m*, H-12'), 2.95(1H, *br s*, H-13'), 2.36(1H, *d*, *J*=11.7 Hz, H-14'), 5.13(1H, *s*, H-17'), 5.69(1H, *s*, H-17'), 0.91(3H, *s*, H-18'), 0.81(3H, *s*, H-19'), 1.00(3H, *s*, H-20') ; $\delta_C$ ($CDCl_3$) 75.1(C-1), 66.7(C-2), 38.6(C-3), 33.3(C-4), 45.6(C-5), 95.1(C-6), 93.3(C-7), 61.4(C-8), 65.4(C-9), 46.6(C-10), 50.9(C-11), 22.9(C-12), 31.9(C-13), 29.4(C-14), 217.2(C-15), 47.2(C-16), 10.7(C-17), 32.7(C-18), 25.0(C-19), 15.7(C-20), 20.9, 20.9, 169.1, 170.4(OAc), 40.1(C-1'), 18.3(C-2' or 6'), 41.4(C-3'), 33.3(C-4'), 54.9(C-5'), 18.4(C-6' or 2'), 33.7(C-7'), 50.7(C-8'), 61.8(C-9'), 38.3(C-10'), 70.9(C-11'), 39.7(C-12'), 36.8(C-13'), 36.8(C-14'), 209.5(C-15'), 149.8(C-16'), 112.8(C-17'), 33.4(C-18'), 21.8(C-19'), 18.0(C-20').

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