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Two Novel Skeletal Diterpenoids, Neodenudatenones A and B, from the Liverwort *Odontoschisma denudatum*

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Abstract: From the ether extract of the liverwort *Odontoschisma denudatum*, two novel diterpenoids, neodenudatenones A and B, having a new carbon skeleton named neodenudatenone-type have been isolated. Their absolute structures were determined by a combination of high resolution 2D-NMR and CD spectra, and chemical degradation.

In our previous paper[1], we reported on the isolation and structure elucidation of three novel *ent*-vibsanine-type diterpenoids named denudatenones A~C (**1**~**3**) with a new dolabellane-type diterpenoid, acetoxyodontoschismenetriol, from the Et_2O extract of the liverwort *Odontoschisma denudatum* as major components.[1] Further fractionation of the Et_2O extract of *O. denudatum* resulted in the isolation of two novel diterpenoids, neodenudatenones A (**4**) and B (**5**) having a new carbon skeleton named neodenudatane-type. We now report on elucidation of their structures.

The ether extract (32.7 g) of dry material (1.25 kg) of *O. denudatum* collected in Tokushima in 1996 was subjected repeatedly to column chromatography on Sephadex LH-20 ($CHCl_3$:MeOH=1:1), silica gel (*n*-hexane-AcOEt, gradient) and HPLC (Chemco sorb 5Si-U; 3% AcOEt-CH_2Cl_2) to afford neodenudatenones A (**4**)[2] (146 mg) and B (**5**)[3] (128 mg) with denudatenones A (**1**) (0.49 g), B (**2**) (1.25g) and C (**3**) (1.05g).

The IR spectrum of neodenudatenone A (**4**) ($C_{20}H_{30}O_2$) indicated the presence of two carbonyl groups (1736 and 1711 cm^{-1}) . The ^1H and ^{13}C NMR spectra of **1** showed the presence of a tertiary methyl [δ_H 1.04 (3H, *s*)], two secondary methyls [δ_H 1.09 (6H, *d*, J= 7.1Hz)], two vinyl methyls [δ_H 1.63, 1.66 (each 3H, *br. s*)], a monosubstituted olefin [δ_H 4.97 (*dd*, J=17.3, 1.1 Hz), 5.00 (*dd*, J=10.7, 1.1 Hz), 5.87 (*dd*, J=17.3, 10.7 Hz)], a disubstituted olefin [δ_H 4.71, 4.91 (each 1H, *br. s*)], a trisubstituted olefin [δ_H 5.02 (*br. d*, J=9.9 Hz)], and two carbonyl groups [δ_C 213.9, 216.1 (each *s*)] as shown in Table 1. Careful analysis of the ^1H-^1H COSY spectrum of **4** suggested the presence of three partial structures (A)~(C) as shown in Figure 1. The new denudatane skeleton was deduced by HMBC along with the HSQC spectra as shown in Table 1. The stereochemistry of **4** was inferred by careful analysis of the NOESY spectrum as shown in Figure 2, and the NOE correlation between H-10 and H-12 indicated that the geometry of the double bond at C-10 was *E*-form. Thus, the relative structure of neodenudatenone A was determined as depicted in formula **4**.

The ^1H and ^{13}C NMR, and IR spectra of neodenudatenone B (**5**) ($C_{20}H_{32}O_2$) were quite similar to those of neodenudatenone A (**4**) except for the observation of a C-12 carbon signal [δ_c 26.1 (*t*)] in high field compared with a C-12 carbon signal [δ_c 33.8 (*t*)] of **4**, and a C-19 carbon signal [δ_c 23.5 (*q*)] in low field compared with a C-19 carbon signal [δ_c 16.9 (*q*)] of **4** as shown in Table 1. The HMBC (Table 1) and NOESY spectra of **5** were quite similar to those of **4** except for NOE between H-10 and H-19 indicating that the geometry of the double bond at C-10 was Z-form. Thus, neodenudatenone B was the geometrical isomer at C-10 of neodenudatenone A as depicted in formula **5**.

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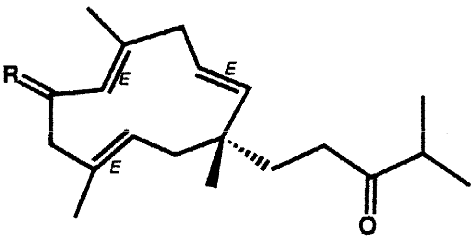

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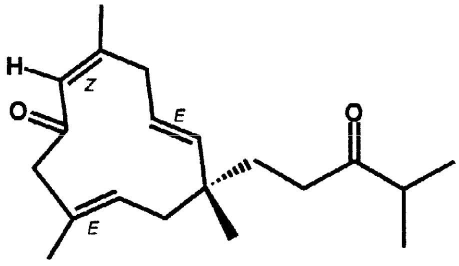
2 R: ═O



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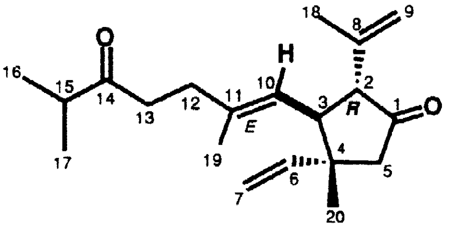

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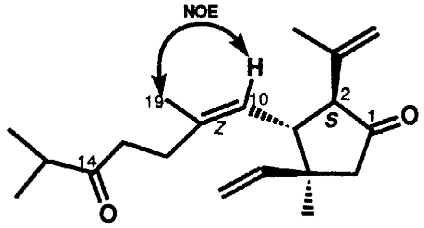

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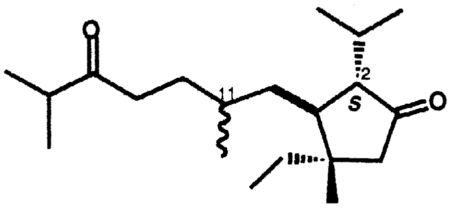

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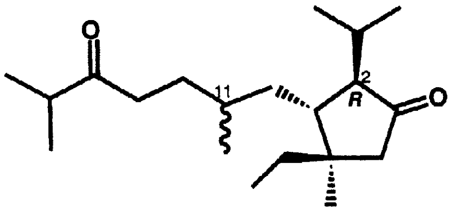

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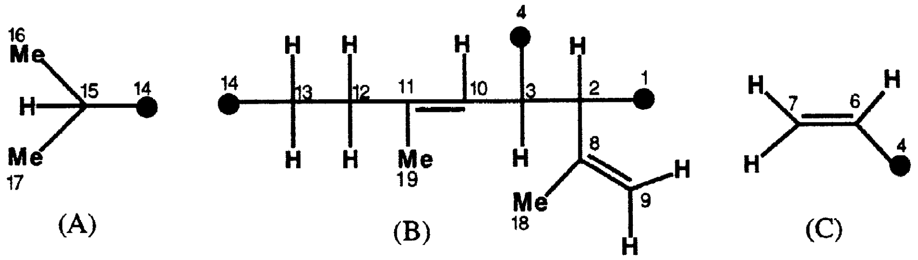


Figure 1. The partial structures of neodenudatenone A (**4**)

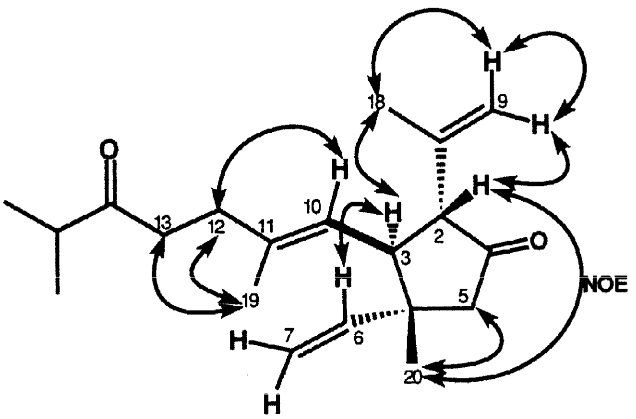
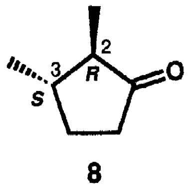


Figure 2. NOE correlations of neodenudatenone A (**4**)



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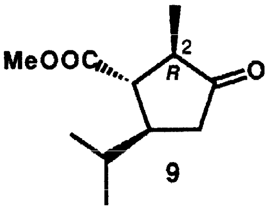

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The absolute configuration of neodenudatenones A (**4**) and B (**5**) was elucidated by experimental results described below. The hydrogenation of **4** and **5** with 10% Pd-C afforded the hexahydrocompounds **6** and **7**. The compounds **6** and **7** were mixtures at C-11, which were very difficult to separate by any separation procedure, and showed the same spectroscopic data except for signs {**6**: $[\alpha]_D^{20}$ +81.1° ($CHCl_3$, c1.06); **7**: $[\alpha]_D^{20}$ -80.1° ($CHCl_3$, c0.89)} of a specific rotation suggesting that compounds **6** and **7** were enatiomeric with each other. The CD spectra of **4** and **6** showed positive single Cotton effects [**4**: 304 nm ($\Delta\varepsilon$ +2.31); **6**: 290 nm ($\Delta\varepsilon$ +1.42)], respectively. The CD spectra of **5** and **7** showed negative single Cotton effects [**5**: 302 nm ($\Delta\varepsilon$ -2.09); **7**: 289 nm ($\Delta\varepsilon$ -1.50)]. Thus, the absolute configurations of C-2 of **6** and **7** were represented as *S* and *R*, respectively, by reference to the CD spectra of cyclopentanone derivatives (**8** and **9**) showing a strong negative Cotton effect at 300 nm.[6,7] Consequently, the absolute configurations of neodenudatenones A and B were thus determined as **4** and **5**, respectively.

Table 1. ^1H NMR (600 MHz), ^{13}C NMR (150 MHz) NMR and HMBC spectra of 4 and 5.*

Compound	Neodenudatenone A (4)		Neodenudatenones A (5)		4 and 5
Carbon	δ_H	δ_C	δ_H	δ_C	HMBC correlations
1		216.1		216.2	
2	2.81 (*dd*, 12.1, 0.8)	61.3	2.80 (*dd*, 11.8, 1.1)	61.5	C-1, 3, 8, 9, 10, 18
3	2.91 (*dd*, 12.1, 9.9)	48.5	2.90 (*dd*, 11.8, 9.9)	48.6	C-2, 4, 6, 8, 11
4		44.1		43.9	
5	2.26 (*dd*, 17.9, 1.4)	52.2	2.26 (*dd*, 17.9, 1.4)	52.5	C-1, 2, 4, 6, 20
	2.39 (*d*, 17.9)		2.37 (*d*, 17.9)		
6	5.87 (*dd*, 17.3, 10.7)	145.2	5.86 (*dd*, 17.3, 10.7)	145.2	C-3, 4, 5, 20
7	4.97 (*dd*, 17.3, 1.1)	112.1	4.98 (*dd*, 17.3, 0.8)	112.4	C-4, 6
	5.00 (*dd*, 10.7, 1.1)		5.00 (*dd*, 10.7, 0.8)		
8		140.4		140.6	
9	4.71 (*br*. s)	115.1	4.72 (*br. s*)	115.3	C-2, 8, 18
	4.91 (*br. s*)		4.92 (*br. s*)		
10	5.02 (*br, d*, 9.9)	122.8	5.00 (*br. d*, 9.9)	123.2	C-2, 3, 4, 12, 19
11		138.4		138.6	
12	2.36 (*t*, 7.7)	33.8	2.23 (*ddd*, 16.7, 10.7, 5.2)	26.1	C-10, 11, 13, 14, 19
			2.30 (*ddd*, 16.7, 10.7, 5.2)		
13	2.54 (*t*, 7.7)	39.2	2.44 (*ddd*, 16.5, 10.7, 5.2)	39.5	C-11, 12, 14, 15
			2.51 (*ddd*, 16.5, 10.7, 5.2)		
14		213.9		214.0	
15	2.60 (*sept*, 7.1)	40.9	2.57 (*sept*, 6.9)	40.9	C-13, 14, 16, 17
16	1.09 (*d*, 7.1)	18.2[a]	1.09 (*d*, 6.9)[b]	18.2[c]	C-14, 15, 17
17	1.09 (*d*, 7.1)	18.3[a]	1.10 (*d*, 6.9)[b]	18.3[c]	C-14, 15, 16
18	1.66 (*br. s*)	20.3	1.66 (*br. s*)	20.3	C-2, 8, 9
19	1.63 (*br. s*)	16.9	1.73 (*br. s*)	23.5	C-10, 11, 22
20	1.04 (*s*)	19.3	1.05 (*s*)	19.0	C-3, 4, 5, 6

* ^1H and ^{13}C NMR spectra were recorded using $CDCl_3$ as solvent and TMS as internal standard. Chemical shifts are in δ values (^1H NMR: δ_H; ^{13}C NMR: δ_C). Coupling constants in Hz are in parenthesis. [a,b,c] Assignments may be interchanged.

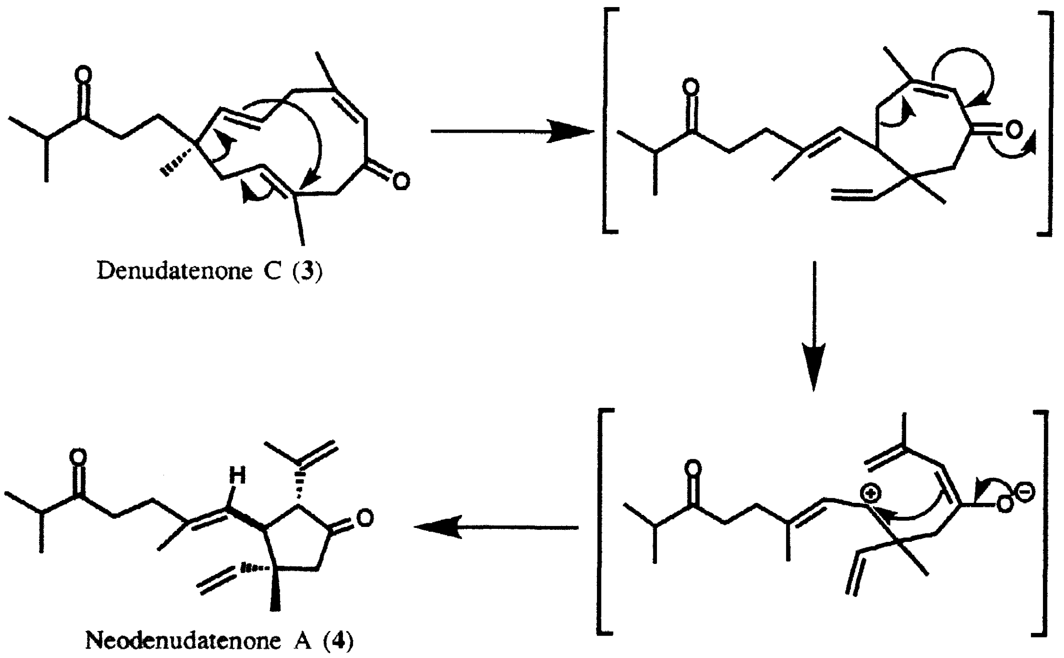

Figure 3. Possible biogenetic pathway of neodenudatenone A (4)

Neodenudatenones A (**4**) and B (**5**) possessing a new carbon skeleton from the liverwort *O. denudatum* are the first examples in nature. It is noteworthy that compounds **4** and **5** were enatiomeric with each other except for the geometry of the double bond in the side chain, and isolated from the same species of liverwort. Neodenudatenones might be biosynthesized from denudatenone C (**3**) by a series of rearrangements as shown in Figure 3.

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References and Notes

1. T. Hashimoto, M. Toyota, H. Koyama, A. Kikkawa, M. Yoshida, M. Tanaka, S. Takaoka and Y. Asakawa, *Tetrahedron Lett.*, **39**, 579 (1998).
2. **4** : colorless oil; $[\alpha]_D^{19}$+73.1° (*c* 1.65, $CHCl_3$); HR-MS: m/z 302.2245, $C_{20}H_{30}O_2$ requires 302.2246; EI-MS: *m/z* 302 (M^+), 203, 136, 120 (100); 71; FT-IR (KBr) cm^{-1}: 1736 (C=O), 1711 (C=O); CD (EtOH): 304 nm (Δε +2.31)
3. **5** : colorless oil; $[\alpha]_D^{19}$ -11.0° (*c* 1.24, $CHCl_3$); HR-MS: m/z 302.2274, $C_{20}H_{30}O_2$ requires 302.2246; EI-MS: *m/z* 302 (M^+), 206, 120 (100); FT-IR (KBr) cm^{-1}: 1736 (C=O), 1711 (C=O); CD (EtOH): 302 nm (Δε -2.09)
4. **6** : colorless oil; $[\alpha]_D^{20}$+81.1° (*c* 1.06, $CHCl_3$); HR-MS: m/z 308.2698, $C_{20}H_{36}O_2$ requires 308.2716; EI-MS: *m/z* 308 (M^+), 293, 265, 167 (100); FT-IR (KBr) cm^{-1}: 1736 (C=O), 1711 (C=O); CD (EtOH): 290 nm (Δε +1.42)
5. **7** : colorless oil; $[\alpha]_D^{20}$ -80.1° (*c* 0.55, $CHCl_3$); HR-MS: m/z 308.2732, $C_{20}H_{30}O_2$ requires 308.2716; EI-MS: *m/z* 308 (M^+), 265, 167 (100); FT-IR (KBr) cm^{-1}: 1736 (C=O), 1711 (C=O); CD (EtOH): 289 nm (Δε -1.50)
6. C. Dierassi, R. Recordes, C. Ouannes and J. Jacques, *Bull. Soc. Chem, France*, 2378 (1966).
7. Y. Asaka, T. Kamikawa and T. Kubota, *Tetrahedron Lett.*, 1597 (1972).