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THREE NEW *ent*-VALERENANE SESQUITERPENES FROM AN OKINAWAN SOFT CORAL

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Three new sesquiterpenes named valerenenol (1), isovalerenenol (2), and anhydrovalerenenol (3), having a new carbon skeleton of *ent*-valerenane, were isolated from an Okinawan soft coral (unidentified sp., Xeniidae) and their absolute stereostructures were elucidated by chemical, physicochemical, and X-ray crystallographic analyses.

KEYWORDS —— *ent*-valerenane sesquiterpene; valerenenol; isovalerenenol; anhydrovalerenenol; soft coral; Xeniidae; ^{1}H NMR; ^{13}C NMR; X-ray analysis; CD

During studies on marine natural products,[1)] we isolated three new *ent*-valerenane sesquiterpenes from an Okinawan soft coral (unidentified sp., Xeniidae). This paper describes the chemical characterization of these sesquiterpenes named valerenenol (1), isovalerenenol (2), and anhydrovalerenenol (3).

The acetone extract of a fresh soft coral collected in July at Kohamajima, Okinawa Prefecture was partitioned by an AcOEt-water solvent system. The AcOEt-soluble portion was subjected to HPLC and preparative GLC separation to furnish 1, 2, and 3 (32%, 2%, and 8% respectively).

The ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of valerenenol (1), colorless oil, $C_{15}H_{26}O$,[2)] $[\alpha]_D$ +123° ($CHCl_3$), IR ($CHCl_3$, cm^{-1}): 3610, showed signals due to two *sec*. CH_3 groups (δ0.85, d, J=6.8 Hz, 8-CH_3; δ0.93, d, J=7.3 Hz, 3-CH_3), two *tert*. CH_3 groups in an isopropanol moiety [δ1.35, 1.37, both s, 12-$(CH_3)_2$], and one olefinic H (δ5.42, br.s, 11-H).[3)] The ^{13}C NMR spectrum (50 MHz) of 1 showed the presence of a trisubstituted double bond (δc 140.7, s, 5-C; δc 134.4, d, 11-C) and a *tert*. OH group (δc 71.3, s, 12-C). Thus, 1 was considered to be a bicarbocyclic sesquiterpene.

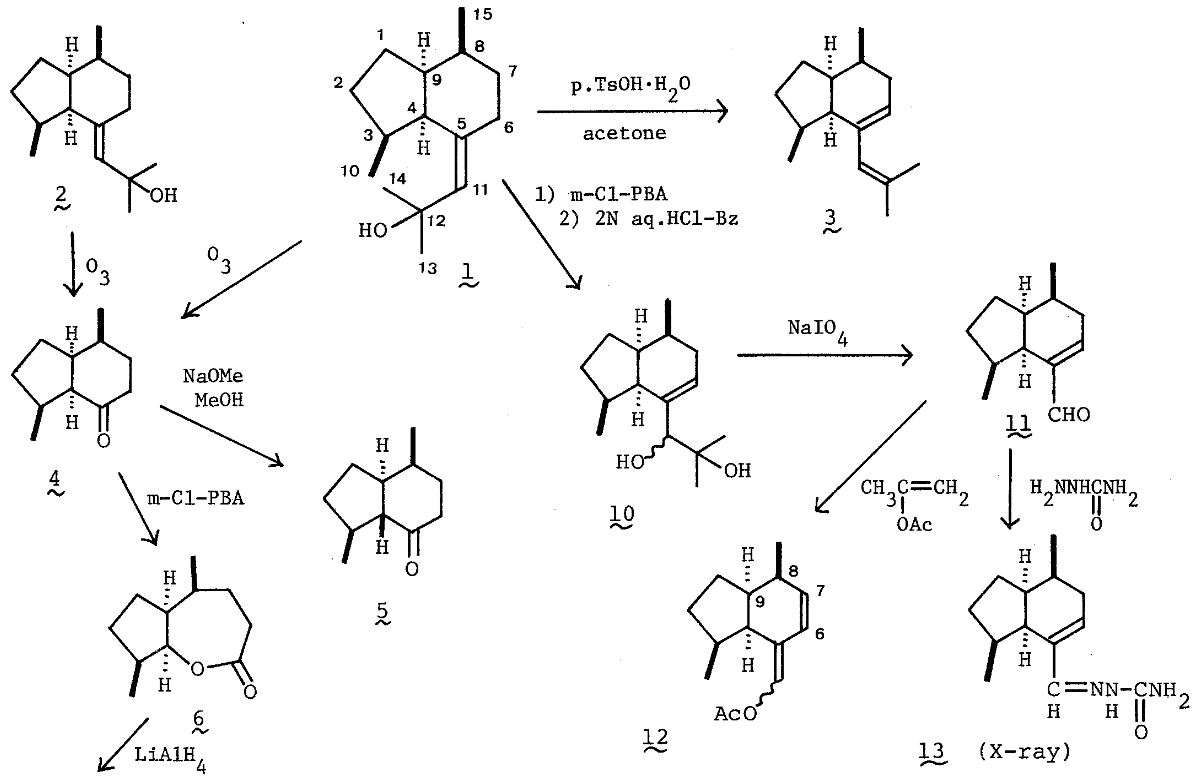
Ozone oxidation of 1 gave an oily tetranor-derivative (4), $C_{11}H_{18}O$, $[\alpha]_D$ +17° ($CHCl_3$), which had a six-membered ring ketone function [IR (CCl_4): 1710; δc 215.2, s, 5-C][4)] and retained two *sec*. CH_3 groups (^{1}H and ^{13}C NMR). *m*-Chloroperbenzoic acid oxidation of this ketone (4) furnished a seven-membered lactone (6), mp 59-60°C, $C_{11}H_{18}O_2$, IR ($CHCl_3$): no OH, 1716, which, on subsequent $LiAlH_4$ reduction, was converted to a cyclopentane diol (**7**), mp 77-78°C, $C_{11}H_{22}O_2$, δ3.91 (1H, br.s, 4-H), 3.60 (2H, br.t, J=6.4 Hz, 5-H_2); δc 76.8 (d, 4-C), 63.5 (t, 5-C), which, after protection of the primary hydroxyl function by *t*-butyldimethylsilylation (giving **7a**), was converted to a cyclopentanone (**8**), $C_{17}H_{34}O_2Si$, IR (CCl_4): 1740, δ3.53 (2H, t, J=6.5 Hz, 5-H_2), δc 223.2 (s, 4-C), 63.5 (t, 5-C). $NaBH_4$ reduction of the ketone (**8**) yielded in 1:1 ratio **7a** and the C-4 epimer (**9**), $C_{17}H_{36}O_2Si$, IR ($CHCl_3$): 3622, δ3.29 (1H, br.t, J=7.3 Hz, 4-H), 3.55 (2H, br.t, J=6.4 Hz, 5-H_2), δc 83.3 (d, 4-C), 63.7 (t, 5-C).

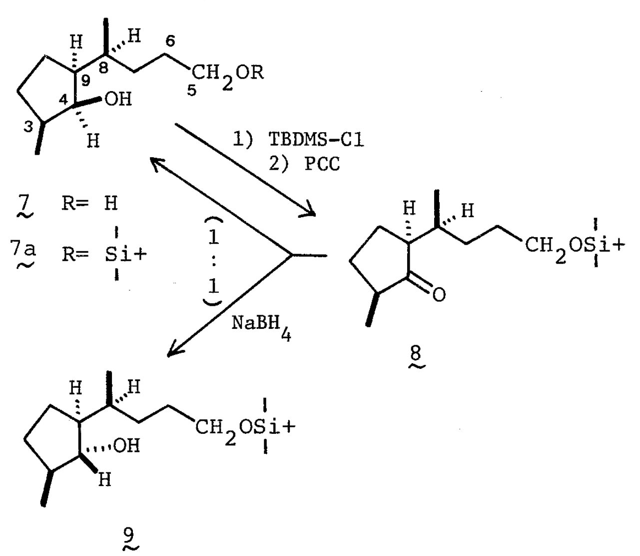
It became clear from the ^{13}C NMR data for **7** and **9** that signals due to 4-C (δc 76.8, d), 10-C (14.3, q) and 8-C (33.4, d) of **7** appeared with higher δ values than **9** (δc 83.3, d; 17.8, q; 36.0, d, respectively) presumably due to steric compression$^{5)}$ by the 4-OH group of **7**. Thus, the neighboring residues at C-3, C-4, and C-9 of the cyclopentane ring of **7** were assumed to be *cis*, whereas those in **9** were *trans* one by one.

Epoxidation followed by acidic treatment (2N HCl-benzene) of **1** quantitatively yielded an epimeric mixture of 5-ene-11,12-diol (**10**), the major product (colorless oil), $C_{15}H_{26}O_2$, IR ($CHCl_3$): 3611, 3573, δ6.60 (1H, br.d, J=7.3 Hz, 6-H), 3.77 (1H, br.s, 11-H), 1.25, 1.18 (both 3H, s, 12-$(CH_3)_2$); δc 142.0 (s, 5-c), 125.8 (d, 6-C), 79.1 (d, 11-C), 73.8 (s, 12-C), 27.1, 24.9 (both q, 13-C, 14-C), which, on subsequent $NaIO_4$ degradation, was converted to the α,β-unsaturated trisnor-aldehyde (**11**), $C_{12}H_{18}O$, UV λ_{max}^{MeOH} 222 nm (ε 10100), δ6.96 (1H, dd, J=2.4, 6.8 Hz, 6-H), 9.41 (1H, s, 11-H), δc 144.2 (s, 5-C), 152.2 (d, 6-C), 194.3 (d, 11-C). Isopropenyl acetate treatment of **11** furnished the enol-acetate (**12**), $C_{14}H_{20}O_2$, UV λ_{max}^{MeOH} 247 nm (ε 17300). The ^1H NMR spectrum of **12** showed signals due to 7-H at δ5.54 (ddd, $J_{7,6}$=9.8, $J_{7,8}$=2.0, $J_{7,9}$=2.0 Hz) and 6-H at δ6.15 (dd, $J_{6,7}$=9.8, $J_{6,8}$=2.0 Hz), thus suggesting the 8β-CH_3 configuration (assuming 4α-H and 9α-H for **1**).

Based on the above-mentioned evidence together with biogenetic consideration, the structure **1** of an *ent*-valerenane skeleton was proposed except the geometry of the 5(11) double bond and the absolute stereochemistry. This was indicated by X-ray crystallographic analysis of the semicarbazone (**13**), mp 207-208°C, which was prepared from **11**. The crystal data and intensity data were derived from measurements on a Syntex R3 four-circle diffractometer with graphite-monochromated Mo Kα radiation. *Crystal data*: $C_{13}H_{21}N_3O$, orthorhombic, space group $P2_12_12_1$, a=7.136(3), b=13.142(9), c=14.694(6) Å, Dx=1.13 g.cm^{-3}, z=4 and μ(Mo Kα)=0.8 cm^{-1}. Intensity data for 952 reflections [I>1.96σ(I)] were collected using an ω-scan mode within 2θ less than 50°. Lorentz and polarization corrections were applied, but no absorption corrections were made. The structure was solved by the direct method using MULTAN on a Syntex XTL program. All the hydrogen atoms were found on a difference Fourier map. The refinement of atomic parameters was carried out by block-diagonal least-squares calculation. The final R-value was 0.056 assuming anisotropic thermal motions for non-hydrogen atoms and isotropic ones for hydrogen atoms. The molecular structure of **13** is illustrated in Fig. 1. The five-membered ring is an envelope type while the six-membered ring is in a distorted half chair form.

The physicochemical properties of isovalerenenol (**2**), colorless semisolid, $C_{15}H_{26}O$, $[\alpha]_D$ +45° ($CHCl_3$), were very similar to those of **1**. Since ozone oxida-





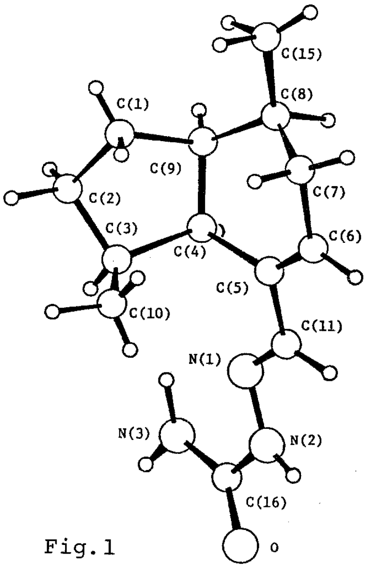


Fig.1

Table I. ^{1}H NMR Data for 1 and 2

		4-H	6α-H	11-H	$3\text{-}CH_3$	$8\text{-}CH_3$	$12\text{-}(CH_3)_2$
1	$CDCl_3$	3.70 (t,J=9.5)	——	5.42	0.93	0.85	1.37
	d_5-Py.	4.11	——	5.57	1.04	0.82	1.53, 1.54
2	$CDCl_3$	2.56 (t,J=8.5)	2.84 (ddd,J=15,9.5,5.5)	5.35	0.90	0.86	1.37
	d_5-Py.	2.56	3.14	5.53	0.95	0.82	1.53.

tion of **2** yielded the same ketone (**4**) as was obtained from **1**, **2** and **1** were shown to be geometrical isomers respectively at the 5(11) double bond.

In order to identify the 5(11)-geometry in **1** and **2**, the solvent-induced shift[6)] in the ^{1}H NMR spectra of both compounds was examined. As shown in Table I, 4-H in **1** and 6α-H in **2** were respectively observed at a lower field in d_5-pyridine than in $CDCl_3$. Thus, the 5(11) double bond in **1** was shown to be *Z*, while that in **2** was *E*. The ^{13}C NMR data for **1** and **2** further supported the assignment by signals due to 4-C (δc 43.5 in **1**; 53.0 in **2**) and 6-C (δc 35.3 in **1**; 25.3 in **2**), which indicated the steric compression due to the C-11 isopropanol moiety onto C-4 in **1** and C-6 in **2**.

The structure of anhydrovalerenenol (**3**), colorless oil, $C_{15}H_{24}$, $[\alpha]_D$ -150° ($CHCl_3$), IR ($CHCl_3$): no OH, UV λ_{max}^{MeOH} 232 nm (ε 7800), was based on its physicochemical properties [*e.g.* δ1.75, 1.76 (both 3H, s, 12-$(CH_3)_2$, 5.50 (1H, s, 11-H), 5.66 (1H, br.d, J=4.6 Hz, 6-H); δc 127.7, 129.2 (both d, 11-C, 6-C), 131.2, 137.7 (both s, 12-C, 5-C)] and its ready formation from **1** by *p*.TsOH-acetone treatment.[7)]

In regard to the absolute stereochemistry of **1**, **2**, and **3**, the CD spectral data for **4**, **12**, and the C-4 epimer of **4** (**5**), which was quantitatively prepared from **4** by alkaline treatment,[8)] gave confirmative evidence: **4**, $[\theta]_{298}$ +2000 (pos. max.); **5**, $[\theta]_{288}$ -3800 (neg. max.); **12**, $[\theta]_{248}$ +35000 (pos. max.). The conformational examination using the Dreiding model disclosed that 3β-CH_3 and 8β-CH_3 in **4** were responsible for the less stable *cis*-indanone structure (**4**) than the *trans*-indanone structure (**5**). Furthermore, the helicity rule[9)] applied to the CD data for **12** supported the absolute stereostructure.

The *ent*-valerenane sesquiterpenes elucidated in this paper are unprecedented examples having a new carbon skeleton, although a few valerenane-type sesquiterpenes were hitherto characterized from *Valeriana officinalis* L.[10)]

REFERENCES AND NOTES

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2) The molecular compositions of compounds with the chemical formulae were determined by elemental analyses and/or high resolution mass spectrometry.
3) The assignments of ^{1}H NMR signals were made on the basis of decoupling experiments in detail.
4) The ketone (**4**) was also obtained from **1** by OsO_4 oxidation and subsequent $NaIO_4$ degradation. Here again, **5** was not formed during the oxidation procedure.
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7) Since the ^{13}C NMR data for **3** resembled those for **11** and **13** except the signals due to their side chain carbons, the C-4 configuration in **1** was considered to be retained in **3** during the dehydration reaction. The ^{13}C NMR data for C-4 isomeric **4** and **5** differed significantly from each other.
8) **4** was also unilaterally isomerized to **5** under strong acidic conditions (c.HCl-acetone), although it was unaffected under mild acidic conditions.
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