Communications to the Editor

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XENIOLONE AND ISOXENIOLONE TWO NEW DITERPENES HAVING A PERHYDROAZULENE SKELETON FROM AN OKINAWAN SOFT CORAL OF *XENIA* SP.

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Two new diterpenes, named xeniolone (1) and isoxeniolone (2), were isolated from an Okinawan soft coral of *Xenia* sp. and their absolute configurations having a perhydroazulene skeleton were determined on the basis of chemical and physicochemical evidence.

KEYWORDS —— xeniolone; isoxeniolone; perhydroazulene diterpene; soft coral; *Xenia* sp.; Horeau's method

Diterpenes with a perhydroazulene skeleton do not occur widely in nature. They have been known so far as constituents of marine brown algae of Dictyotaceae[1] and the sea hare *Aplysia depilans*,[2] which is known as a predator on those brown algae. In searching for new chemical constituents in marine organisms,[3] we have investigated an Okinawan soft coral of *Xenia* sp. and have isolated two new diterpenes named xeniolone (1) and isoxeniolone (2) which comprise a perhydroazulene skeleton. This paper deals with the evidence which is consistent with their absolute configurations.[4]

An acetone extract of the fresh soft coral (collected in July at Zamami-jima, Okinawa Prefecture) was partitioned in a water-AcOEt mixture. The AcOEt soluble portion was subjected to silica gel column chromatography (hexane-AcOEt) to afford a diterpene fraction, which gave a single spot on ordinary TLC. Two constituents of the diterpene fraction were separated by HPLC (Cosmosil $5C_{18}$, MeOH-H_2O) to furnish xeniolone (1) and isoxeniolone (2) in 2 and 1.5% yields respectively from the AcOEt extract.

Xeniolone (1), a colorless oil, $C_{20}H_{32}O_2$,[5] $[\alpha]_D$ -20° ($CHCl_3$), showed hydroxyl (3600, 3450 cm^{-1}) and carbonyl (1705 cm^{-1}) absorption bands in its IR spectrum ($CHCl_3$). The ^{1}H-NMR (500 MHz, d_5-pyridine) and ^{13}C-NMR (22.5 MHz)[6] spectra of 1 showed the presence of a trisubstituted double bond (δ 5.99, 1H d, J=3.0 Hz, 6-H), a terminal methylene group (δ 4.88, 4.85, both 1H s, 18-H_2), a methyl group attached to a carbon bearing a hydroxyl group(δ 1.46, 3H s, 4-CH_3), and three secondary methyl groups [δ 1.04, 3H d, J=7.0 Hz, 11-CH_3; 0.88, 6H d, J=6.5 Hz, 15-$(CH_3)_2$]. Thus, a bicarbocyclic diterpene skeleton of 1 has been elucidated.

Isoxeniolone (2), a colorless oil, $C_{20}H_{32}O_2$, $[\alpha]_D$ +31° ($CHCl_3$), IR ($CHCl_3$): 3600, 3450, 1705 cm^{-1}, gave a spot identical to xeniolone (1) on TLC (*e.g.* precoated silica gel 60 F_{254}, Merck, Rf=0.5, hexane-AcOEt=2:1). The ^{13}C-NMR[6] and ^{1}H-NMR (d_5-pyridine) spectra of 2 were very similar to those of 1: *e.g.* δ 6.00 (1H d, J=3.0 Hz), 4.87, 4.83 (both 1H s), 1.44 (3H s), 1.03 (3H d, J=7.0 Hz), 0.88, 0.87 (both 3H d, J=6.5 Hz).

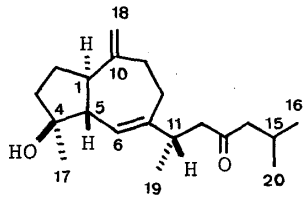
Respective dehydrogenation of xeniolone (1) and isoxeniolone (2) over 10% Pd-C in xylene containing I_2 (reflux, 2 h)[7] yielded an identical azulene (3),[8] $C_{20}H_{26}O$, λ_{max}^{MeOH} nm (ε): 655 (300), 603 (350), IR ($CHCl_3$): 1705 cm^{-1} in high yield. Acetylation (Ac_2O/pyridine/AgCN, 90°C, 4 h)[9] followed by photosensitized oxygenation (Rose Bengal/O_2/acetone-pyridine (10:1)/100 W high pressure Hg lamp/in Pyrex tube/0°C, 1 h)[7,10] of 1 and 2 provided 4, a colorless oil, $C_{22}H_{34}O_4$, δ ($CDCl_3$) 2.31 (1H m, 1α-H), 3.15 (1H dd, J=10.5, 10.5 Hz, 5β-H), 4.22 (1H d, J=10.5 Hz, 6α-H), 5.64 (1H dd, J=9.5, 4.5 Hz, 8-H), 3.28 (1H br d, J=15.5 Hz, 9α-H), 2.67 (1H dd, J=15.5, 9.5 Hz, 9β-H), and 5, a colorless oil, $C_{22}H_{34}O_4$, δ ($CDCl_3$) 2.31 (1H m, 1β-H), 3.05 (1H dd, J=10.5, 10.5 Hz, 5α-H), 4.41 (1H d, J=10.5 Hz, 6β-H), 5.71 (1H dd, J=9.5, 4.5 Hz, 8-H), 3.26 (1H br d, J=15.5 Hz, 9β-H), 2.71 (1H dd, J=15.5, 9.5 Hz, 9α-H), as respective major products.

Based on the above-mentioned evidence together with biogenetic consideration, xeniolone (1) and isoxeniolone (2) have been considered to be two diastereomeric diterpenes having a perhydroazulene skeleton.

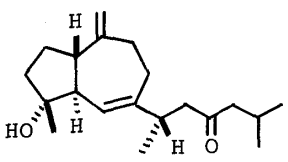
Treatment of isoxeniolone (2) with $NaOCH_3$-CH_3OD furnished a tetradeutero derivative, which gave an ion peak at *m/z* 204 assignable to $[M - CD_2{=}C(OH){-}CD_2{-}CH(CH_3)_2]^+$, thus the side chain structure (C_{12-16}, C_{20}) of 2 with a 13-CO moiety being suggested. Furthermore, $NaBH_4$ reduction of 2 furnished a mixture (*ca.* 1:1) of two diastereomeric diols (6). Each diol, $C_{20}H_{34}O_2$, was separated by silica gel column chromatography and subjected to tosylation and subsequent DBU treatment to provide two trienes as colorless oils: 7, $C_{20}H_{32}O$, δ ($CDCl_3$) 5.39 (1H dt, J=15.5, 6.5 Hz), 5.33 (1H dd, J=15.5, 6.0 Hz) and 8, $C_{20}H_{32}O$, δ ($CDCl_3$) 5.36 (1H dd, J=15.5, 6.0 Hz), 5.28 (1H dt, J=15.5, 7.5 Hz). In the ^{1}H-NMR spectrum (d_5-pyridine) of 7, 1-H and 5-H were shown to couple with J=12 Hz. When the 11-CH_3 signal was irradiated, 11% and 8% NOE were observed on 11-H and 6-H signals, whereas, upon irradiation of the 4β-CH_3 signal, 10% and 7% NOE were observed on 6-H and 1-H signals, respectively. Thus, the relative configurations at C-1, C-4, and C-5 of isoxeniolone have been elucidated as shown in 2.

Oxidation of xeniolone (1) and isoxeniolone (2) with OsO_4-$NaIO_4$ respectively yielded isomeric nordiketones: 9, $C_{19}H_{30}O_3$, $[\alpha]_D$ -58° ($CHCl_3$), δ (d_5-pyridine) 3.07 (1H m, 1-H), 2.77 (1H br d, J=12.0 Hz, 5-H) and 10, $C_{19}H_{30}O_3$, $[\alpha]_D$ +40° ($CHCl_3$), δ (d_5-pyridine) 3.07 (1H m), 2.76 (1H br d, J=12.5 Hz). The CD spectrum of 9 (MeOH) showed a negative maximum at 285 nm (θ: -5300) due to the 10-CO $n \rightarrow \pi^*$ transition, whereas 10 showed a positive CD maximum of $[\theta]_{285}$ +6100. Consequently, the structures of xeniolone (1) and isoxeniolone (2) have been elucidated, except for their C-11 configurations which are identical in both compounds.[11]

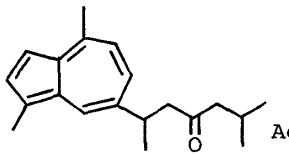
In order to determine the common C-11 configuration in xeniolone (1) and isoxeniolone (2), 1 and 2 were treated with CH_3MgI to provide a diol mixture (11), $C_{21}H_{36}O_2$, δ ($CDCl_3$) 1.15 (3H s, 13-CH_3). The mixture was then subjected to successive treatment: i) ozone oxidation (hexane-AcOEt-pyridine, -78°C), ii) Baeyer-



xeniolone (1)



isoxeniolone (2)



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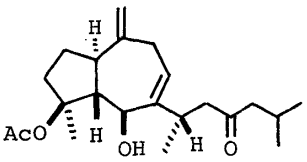

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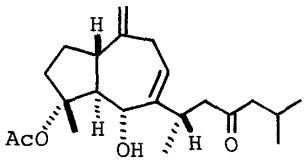

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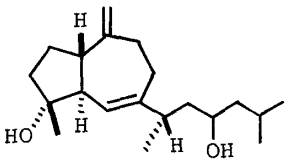

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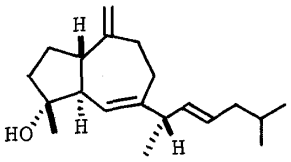

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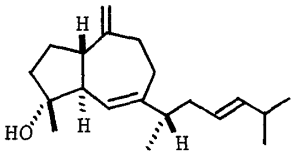

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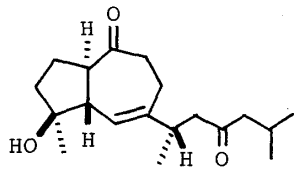

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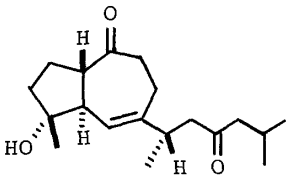

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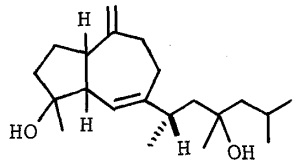

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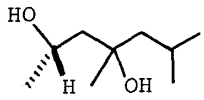

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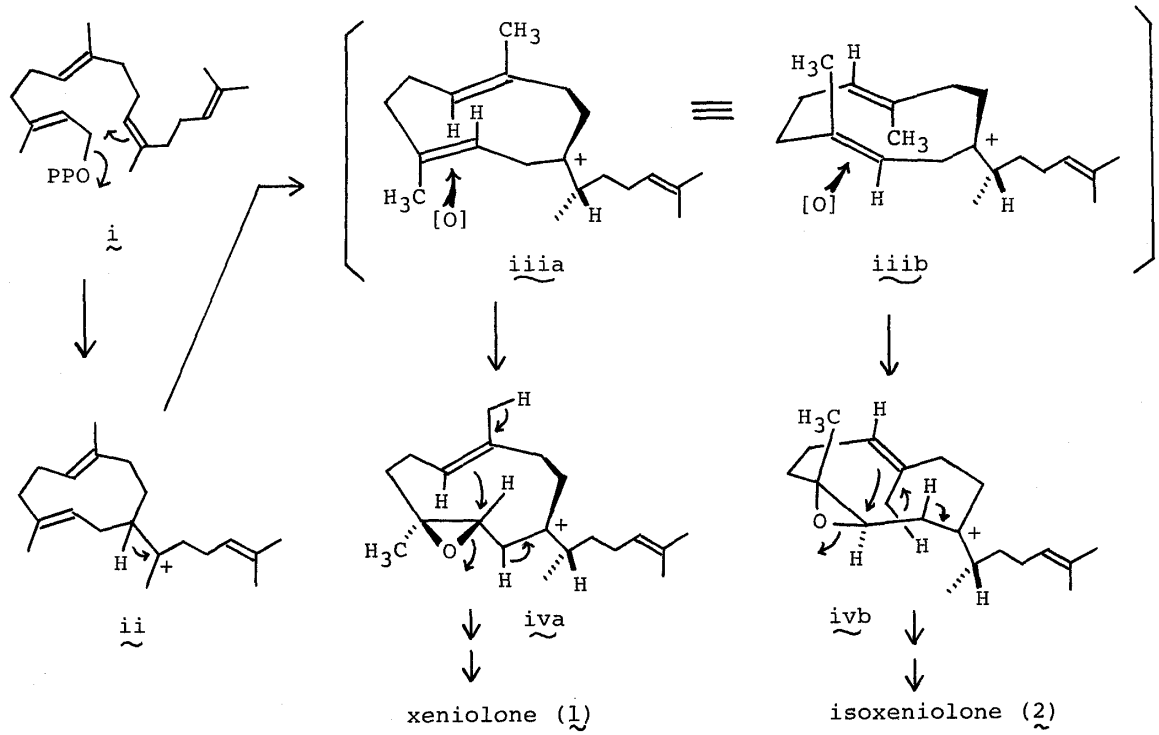
Hypothetical Biogenetic Pathway



Villiger oxidation (*m*-Cl-perbenzoic acid-$CHCl_3$/20°C, 60 h), and iii) alkaline hydrolysis, to yield a diol (12), $C_9H_{20}O_2$. Application of the Horeau's method[12] to 12 resulted in the liberation of α-phenylbutyric acid of $[\alpha]_D$ -1.9° (benzene), which confirmed the 2S configuration in 12. Thus, the 11S configurations in 1 and 2 have been determined.

Based on the above-mentioned evidence, the total structures of xeniolone and isoxeniolone have been elucidated as 1 and 2. In regard to the biogenetic pathway of xeniolone (1) and isoxeniolone (2), the scheme shown on the previous page seems to be attractive. This appears to be a rare example of co-occurring isomeric diterpenes which are presumably biosynthesized through two different diastereoselective epoxidations (iiia, iiib).

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4) Presented at the 28th Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics (Kanazawa, Oct. 13., 1984) by M. Kobayashi, Cai Yang, I. Kitagawa, and Y. Kyogoku. Abstract Papers p. 48.
5) The molecular compositions of compounds with the chemical formulae were determined by high resolution mass spectrometry.
6) ^{13}C-NMR (22.5 MHz, $CDCl_3$, δc): xeniolone (1): 47.0 (d, C-1), 80.5 (s, C-4), 54.9 (d, C-5), 123.6 (d, C-6), 146.8 (s, C-7), 153.4 (s, C-10), 38.9 (d, C-11), 49.0 (t, C-12), 210.1 (s, C-13), 52.2 (t, C-14), 24.4 (d, C-15), 22.7 (2C, q, C-16,20), 24.1 (q, C-17), 106.7 (t, C-18), 19.5 (q, C-19), 40.0, 36.8, 30.1, 24.8 (each t, C-2,3,8,9) and isoxeniolone (2): 47.0 (d, C-1), 80.5 (s, C-4), 54.9 (d, C-5), 123.7 (d, C-6), 146.7 (s, C-7), 153.4 (s, C-10), 39.1 (d, C-11), 49.0 (t, C-12), 210.1 (s, C-13), 52.2 (t, C-14), 24.4 (d, C-15), 22.7 (2C, q, C-16,20), 24.1 (q, C-17), 106.7 (t, C-18), 19.7 (q, C-19), 40.0, 36.8, 29.8, 24.8 (each t, C-2,3,8,9).
7) M. Kobayashi, B. W. Son, Y. Kyogoku, and I. Kitagawa, Chem. Pharm. Bull., 32, 1667 (1984).
8) Presumably racemic, although the optical rotation could not be measured due to its deep blue color.
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