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TWO NEW XENICANE DITERPENOIDS FROM OKINAWAN SOFT CORAL OF THE GENUS, *XENIA*

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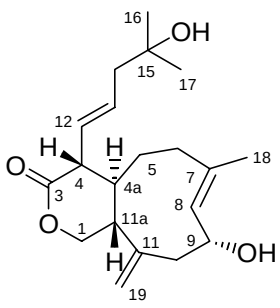
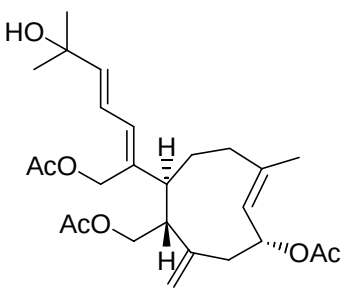
Abstract - Two new xenicane diterpenoids, dihydroxeniolide-A and isoxeniatriacetate, were isolated from Okinawan soft coral of the genus, *Xenia*. The relative configurations of two new xenicane diterpenoids were determined based on spectroscopic analysis. The absolute configuration of dihydroxeniolide-A was determined using the modified Mosher's method. The absolute configuration of isoxeniatriacetate was determined by chemical conversion.

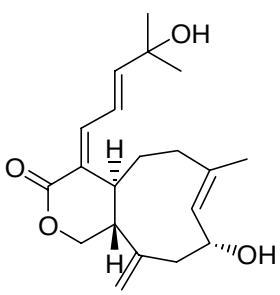
Soft coral of the genus *Xenia* is a rich source of xenicane diterpenoids which possess unique structural features and biological activity.[2,3] The isolation and structural determinations of xenicane diterpenoids from the Okinawan soft coral *Xenia* sp. were reported in our previous papers.[4,5] Subsequent study on chemical constituents of Okinawan soft coral led to the isolation of new xenicane diterpenoids, dihydroxeniolide-A (**1**) and isoxeniatriacetate (**2**), from a soft coral of the genus of *Xenia* along with xeniolide-A[6] (**3**), xeniolide-B,[6] and xenialactol.[7,8] In the following, the isolation and structural determinations of dihydroxeniolide-A (**1**) and isoxeniatriacetate (**2**) are discussed.



dihydroxeniolide-A (**1**)



isoxeniatriacetate (**2**)



xeniolide-A (**3**)

Dihydroxeniolide-A (**1**) was found to have the molecular formula $C_{20}H_{30}O_4$ based on HREIMS. The IR spectrum of **1** indicated absorptions due to a hydroxy group (3500 cm^{-1}) and δ-lactone (1735 cm^{-1}). All twenty carbons appeared in the ^{13}C NMR and DEPT spectra disclosed the presence of three methyls, five sp^3 methylenes, one sp^2 methylene, four sp^3 methines, three sp^2 methines, one sp^3 quaternary carbon and three sp^2 quaternary carbons (Table 1). ^1H and ^{13}C NMR spectral correlations were demonstrated by the HMQC spectrum. ^1H and ^{13}C NMR spectra showed the presence of one *E*-disubstituted olefin [δ_H 5.53 (1H, d, J = 7.5 Hz), δ_C 130.7 (CH), 132.8 (C)], one *exo* methylene [δ_H 4.88 (1H, br s), 5.02 (1H, br s), δ_C 115.6 (CH_2), 148.7 (C)], one olefinic methyl [δ_H 1.68 (3H, s), δ_C 17.3 (CH_3)], two methyls [δ_H 1.21 (3H, s), 1.24 (3H, s), δ_C 29.0 (CH_3), 29.4 (CH_3)], one oxygenated quaternary carbon [δ_C 70.5 (C)], one oxygenated methine adjacent to trisubstituted olefin [δ_H 4.72 (1H, br t, J = 6.6 Hz), 5.18 (1H, d, J = 7.5

Table 1. NMR spectral data for dihydroxeniolide-A (**1**) and isoxeniatriacetate(**2**).

	1		**2**	
No.	^{13}C NMR[a]	^1H NMR (J in Hz)[b]	^{13}C NMR[c]	^1H NMR (J in Hz)[d]
1	67.7 (CH_2)	4.06 (dd, 11.5, 2.8)	64.9 (CH_2)	3.80 (dd, 11.5, 10.4)
		4.19 (dd, 11.5, 3.9)		4.04 (dd, 11.5, 4.9)
3	174.2 (C)	-	60.9 (CH_2)	4.71 (d, 12.6)
		-		4.76 (d, 12.6)
4	49.5 (CH)	2.88 (dd, 9.6, 8.0)	120.5 (C)	-
4a	46.0 (CH)	1.82 (m)	46.9 (CH)	2.28 (m)
5	34.9 (CH_2)	1.46 (m)	33.2 (CH_2)	1.47 (m)
		1.87 (m)		1.63 (m)
6	39.5 (CH_2)	2.17 (dt, 12.6, 3.5)	39.7 (CH_2)	1.89 (m)
		2.24 (dt, 4.3, 12.6)		1.99 (m)
7	132.8 (C)	-	138.1 (C)	-
8	130.7 (CH)	5.18 (d, 7.5)	124.0 (CH)	5.27 (d, 10.1)
9	67.0 (CH)	4.72 (br t, 6.6)	72.4 (CH)	5.52 (m)
10	46.0 (CH_2)	2.38 (dd, 13.7, 1.2)	36.5 (CH_2)	1.96 (m)
		2.43 (dd, 13.7, 6.0)		2.57 (dd, 12.8, 5.2)
11	148.7 (C)	-	142.1 (C)	-
11a	48.4 (CH)	1.79 (m)	52.3 (CH)	2.46 (dt, 4.9, 10.4)
12	130.1 (CH)	5.53 (dd, 15.5, 8.0)	131.0 (CH)	6.08 (d, 11.0)
13	131.3 (CH)	5.62 (dt, 15.5, 7.2)	121.5 (CH)	6.44 (dd, 15.2, 11.0)
14	46.6 (CH_2)	2.27 (d, 7.2)	143.6 (CH)	5.88 (d,15.2)
15	70.5 (C)	-	70.8 (C)	-
16	29.0 (CH_3)	1.21 (s)	29.7 (CH_3)	1.35 (s)
17	29.4 (CH_3)	1.24 (s)	29.7 (CH_3)	1.35 (s)
18	17.3 (CH_3)	1.68 (s)	19.5 (CH_3)	1.69 (s)
19	115.6 (CH_2)	4.88 (br s)	120.1 (CH_2)	5.00 (br s)
		5.02 (br s)		5.02 (br s)
1-Ac			21.3 (CH_3)	2.06 (s)
			170.6 (C)	-
3-Ac			21.0 (CH_3)	2.09 (s)
			171.0 (C)	-
9-Ac			20.9 (CH_3)	1.94 (s)
			170.6 (C)	-

[a] 100 MHz, $CDCl_3$, [b] 400 MHz, $CDCl_3$, [c] 125 MHz, $CDCl_3$, [d] 500 MHz, $CDCl_3$

Hz), δ_C 67.0 (CH), 130.7 (CH), 132.8 (C)], one oxygenated methylene [δ_H 4.06 (1H, dd, *J* = 11.5, 2.8 Hz), 4.19 (1H, dd, *J* = 11.5, 3.9 Hz), δ_C 67.7 (CH_2)] and lactone carbonyl [δ_C 174.2 (C)]. The above functional groups were extended to the partial structures, -O-CH_2-CH- (C-1 and C-11a), -CH-CH=CH-CH_2- (C-4, C-12, C-13 and C-14), -CH-CH_2-CH_2- (C-4a, C-5 and C-6) and –C(CH_3)=CH-CH(OH)-CH_2- (C-7, C-18, C-8, C-9 and C-10) according to the COSY spectrum. These partial structures and the other functional groups were connected together based on the HMBC spectrum; also observed were following the cross peaks: H-1/C-3; H-4/C-3, C-4a; H-4a/C-11a; H-6/C-7; H-10/C-11; H-11a/C-11; H-14/C-15; Me-16/C-15 and Me-17/C-15. Based on these findings, it was thus possible to construct the xenicane skeleton. The *E* configuration of the carbon-carbon double bond at C-7 position was indicated by ^{13}C chemical shift (δ_C 17.3, CH_3) of the olefinic methyl group[9] at the C-18 position and NOE correlations between H-9 (δ_H 4.72) and Me-18 (δ_H 1.68) (Figure 1).

Relative configurations of all chiral centers in **1** were clarified from the NOESY spectrum (Figure 1). *trans*-Juncture of two rings was indicated by NOE correlations between H-4 (δ_H 2.88) and H-11a (δ_H 1.79) and between H-4a (δ_H 1.82) and H-19 (δ_H 4.88), suggesting H-4 and H-11a to be on the same face of the ring and H-4a and the *exo* methylene moiety to be on the opposite face to H-11a. Conformation of the 9-membered ring was inferred based on NOE correlations between H-4a and H-8 (δ_H 5.18) and between H-8 and H-19 (δ_H 5.02) and between H-11a and Me-18 (δ_H 1.68). Stereochemistry of the hydroxy group at C-9 was found to shown an α configuration by NOE correlation between H-9 (δ_H 4.72) and H-18. The relative configuration of **1** was thus assigned to 4*R**, 4a*S**, 9*R** and 11a*R**. The absolute configuration of **1** was determined by application of the modified Mosher's method.[10] Dihydroxeniolide-A (**1**) was converted to (*R*)-MTPA ester and (*S*)-MTPA ester, respectively. The ^1H NMR spectrum of each MTPA ester was measured and Figure 2 shows the value of Δδ. The signs are positive due to left-sided protons but negative owing to right-sided protons, thus demonstrating the 9*R* configuration. The present results indicate 4*R*, 4a*S*, 9*R* and 11a*R* for **1**.

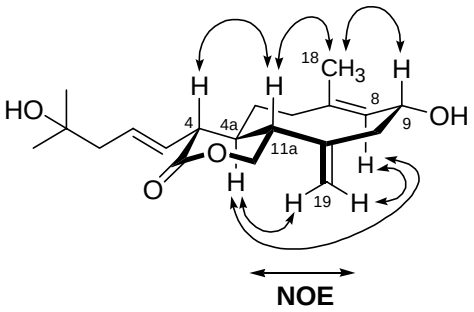
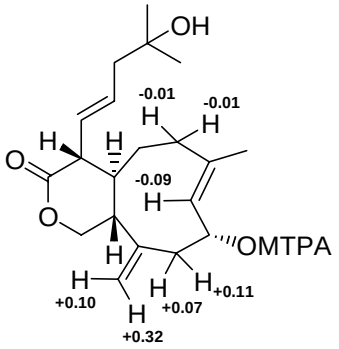


Figure 1. Selected NOE correlations of **1**.



Δδ = δ (*S*)-MTPA ester - δ (*R*)-MTPA ester

Figure 2. Δδ obtained for the MTPA ester of **1**.

Isoxeniatriacetate (**2**) was shown to have the molecular formula $C_{26}H_{38}O_7$ based on HREIMS. The IR spectrum of **2** indicated absorptions due to a hydroxy group (3391 cm^{-1}) and ester carbonyl (1737 cm^{-1}).

The conjugated diene group (-CH=CH-CH=C-) could be seen from the UV spectrum [λ_{max} 244 nm (ε 29,000)]. All twenty-six carbons appeared in the ^{13}C NMR and DEPT spectra indicated six methyls, five sp^3 methylenes, one sp^2 methylene, three sp^3 methines, four sp^2 methines, one sp^3 quaternary carbon and six sp^2 quaternary carbons to be presented (Table 1). ^{1}H and ^{13}C NMR correlations were evident from the HMQC spectrum. ^{1}H and ^{13}C NMR spectra disclosed three acetyl groups [δ_H 1.94 (3H, s), 2.06 (3H, s), 2.09 (3H, s), δ_C 170.6 (C), 170.6 (C), 171.0 (C)], one conjugated diene group (-CH=CH-CH=C-) [δ_H 5.88 (1H, d, *J* = 15.2 Hz), 6.08 (1H, d, *J* = 11.0 Hz), 6.44 (1H, dd, *J* = 15.2, 11.0 Hz) δ_C 120.5 (C), 121.5 (CH), 131.0 (CH), 143.6 (CH)], one *exo* methylene [δ_H 5.02 (1H, br s), 5.02 (1H, br s), δ_C 120.1 (CH_2), 142.1 (C)], one olefinic methyl [δ_H 1.69 (3H, s), δ_C 19.5 (CH_3)], two methyls [δ_H 1.65 (3H, s), 1.35 (3H, s), δ_C 29.7 (CH_3), 29.7 (CH_3)], one oxygenated quaternary carbon [δ_C 70.5 (C)], one oxygenated methine adjacent to trisubstituted olefin [δ_H 5.27 (1H, d, *J* = 10.1 Hz), 5.52 (1H, m), δ_C 72.4 (CH), 124.0 (CH), 138.1 (C)] and two oxygenated methylenes [δ_H 3.80 (1H, dd, *J* = 11.5, 10.4 Hz), 4.04 (1H, dd, *J* = 11.5, 4.9 Hz), δ_C 64.9 (CH_2); δ_H 4.71 (1H, d, *J* = 12.6 Hz), 4.76 (1H, d, *J* = 12.6 Hz), δ_C 60.9 (CH_2)]. The above functional groups were extended to the partial structures, -O-CH_2-CH-CH-CH_2- (C-1, C-11a, C-4a and C-5), -C=CH-CH=CH- (C-4, C-12, C-13 and C-14) and -C(CH_3)=CH-CH(OAc)-CH_2-C=CH_2 (C-7, C-18, C-8, C-9, C-10, C-11 and C-19) based on the COSY spectrum. These partial structures and the other functional groups were found to be connected based on the HMBC spectrum; also observed were included the cross peaks: H-1/1-Ac; H-3/3-Ac, C-4; H-4a/C-4, C-12; H-6/C-4a, C-5, C-7, C-8, Me-18; H-9/9-Ac; H-11a/C-11 and H-14/C-15, so that the xenicane skeleton could be constructed. The *E* configuration of the carbon-carbon double bond at C-7 position was indicated by ^{13}C chemical shift (δ_C 19.5, CH_3) of the olefinic methyl group[8] at the C-18 position and NOE correlations between H-9 (δ_H 5.52) and Me-18 (δ_H 1.69). The *Z* configuration of the carbon-carbon double bond at C-4 position was indicated by the NOE correlations between H-3 (δ_H 4.71 and 4.76) and H-13 (δ_H 6.44) and between H-4a (δ_H 2.28) and H-12 (δ_H 6.08) (Figure 3).

Relative configurations of all chiral centers in **2** were elucidated based on the NOESY spectrum (Figure 3). NOE correlations between H-11a (δ_H 2.46) and H-19 (δ_H 5.00), among H-9 (δ_H 5.52), H-18 (δ_H 1.69) and H-19 (δ_H 5.02) and between H-4a (δ_H 2.28) and H-8 (δ_H 5.27), which suggested H-9 and H-11a to be on the same face of the 9-membered ring and H-4a to be on the opposite face to H-11a. The relative configuration of **2** was thus assigned to 4a*S**, 9*R** and 11a*R**.

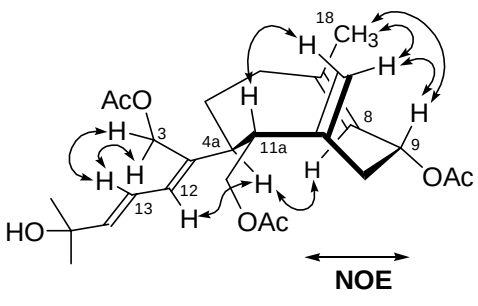
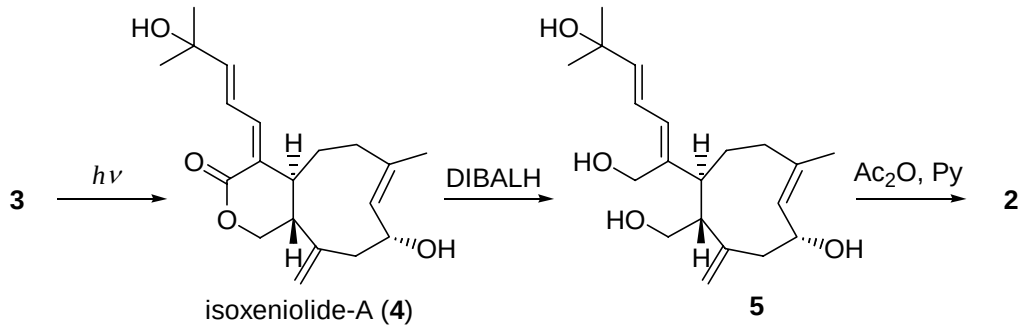


Figure 3. Selected NOE correlations of **2**.

The absolute configuration of isoxeniatriacetate (**2**) was determined by chemical conversion of xeniolide-A (**3**) to isoxeniatriacetate (**2**) (Scheme 1). A solution of xeniolide-A (**3**) in benzene was irradiated with a high pressure mercury lump to provide isoxeniolide-A (**4**), $[\alpha]^{20}_{D}$ +41.0° (*c* 0.40, MeOH), lit.$[\alpha]_{D}$ +50° (*c* 0.655, MeOH).[11] Isoxeniolide-A (**4**) was reduced with DIBALH in THF at –78°C to give tetraol (**5**), $[\alpha]^{27}_{D}$ –184° (*c* 0.90, $MeOH_3$). Treatment of tetraol (**5**) with acetic anhydride and pyridine afforded triacetate (**2**), $[\alpha]^{22}_{D}$ –178° (*c* 0.09, $CHCl_3$). Spectral data and sign of optical rotation of synthesized **2** were identical to those of natural isoxeniatriacetate (**2**). This conversion demonstrated the absolute configuration of **2** to be 4a*S*, 9*R* and 11a*R*.



Scheme 1. Chemical conversion of xeniolide-A (**3**) to isoxeniatriacetate (**2**).

EXPERIMENTAL

General Experimental Procedures. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter and IR spectra were taken with a Perkin-Elmer FT-IR 1710 spectrophotometer or JASCO A-302 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker AM-400 or AM-500. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as the internal standard. EIMS and HREIMS spectra were obtained with a VG Auto Spec spectrometer.

Animal Material, Extraction and Isolation. Soft coral *Xenia* sp. was collected from the coral reef of Ishigaki Island (Okinawa, Japan) in May 1992 at a depth of 1-3 m. A voucher specimen (SC-II-1) is deposited at this laboratory, School of Pharmacy, Tokyo University of Pharmacy and Life Science (Tokyo, Japan). Wet specimens (8.0 kg) were immersed in MeOH (5.0 L x 3) at rt for 24 h and MeOH extracts (222 g) were partitioned between EtOAc (1.5 L x 2) and H_2O (1.5 L) to give EtOAc-soluble portions (14.1 g). A part (7.9 g) of the EtOAc-soluble portions was chromatographed on a silica gel column to give the following fractions; fraction 1 (1.4 g) eluted with hexane-EtOAc = 10 : 1 (1.0 L), fraction 2 (1.7 g) eluted with hexane-EtOAc = 3 : 1 (1.0 L), fraction 3 (3.6 g) eluted with EtOAc (1.0 L) and fraction 4 (1.2 g) eluted with MeOH (1.0 L). Fraction 3 was subjected to flash silica gel column chromatography (hexane-EtOAc = 3 : 1), providing fractions 3-1 (1.86 g), 3-2 (880 mg), 3-3 (790 mg) and 3-4 (70 mg). Fraction 3-1, by repeated flash silica gel column chromatography (hexane-EtOAc =

6 : 5 for the first chromatography and hexane-EtOAc = 3 : 2 for the second chromatography) gave fractions 3-1-1 (104 mg), 3-1-2 (73 mg) and 3-1-3 (55 mg). Fraction 3-1-2 subjected to normal phase HPLC (hexane-EtOAc = 2 : 1) gave isoxeniatriacetate (**2**) (11.0 mg). From fraction 3-2 *via* to repeated flash silica gel column chromatography ($CHCl_3$-acetone = 3 : 1) xeniolide-A[6] (**3**) (634 mg) and fraction 3-2-2 (246 mg) were obtained. Fraction 3-2-2 was subjected to normal phase HPLC ($CHCl_3$-MeOH = 30 : 1) and flash ODS column chromatography (MeOH-H_2O = 3 : 1) followed by normal phase HPLC (hexane-EtOAc = 2 : 3) to give dihydroxeniolide-A (**1**) (14 mg). Fraction 3-3 was subjected to normal phase HPLC ($CHCl_3$-MeOH = 30 : 1) and flash ODS column chromatography (MeOH-H_2O = 3 : 1) followed by normal phase HPLC (hexane-EtOAc = 1 : 2) to give xeniolide-B[6] (9.0 mg). Fraction 3-4 was subjected to flash silica gel column chromatography ($CHCl_3$-acetone = 2 : 1) to give xenialactol[7,8] (21 mg).

Dihydroxeniolide-A (1): Colorless oil; $[\alpha]^{25}_D$ –31.2° (*c* 1.21, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3500, 1735, 1640 cm^{-1}; ^1H and ^{13}C NMR spectra see Table 1; HMBC correlation (H/C) 3/1, 3/4, 3/4a, 3/12, 4a/3, 4a/4, 4a/5, 4a/6, 4a/11a, 4a/12, 6/4a, 6/5, 6/7, 6/8, 6/18, 8/6, 8/9, 8/18, 9/7, 9/8, 9/10, 10/8, 10/9, 10/11, 10/11a, 10/19, 11a/1, 11a/4, 11a/4a, 11a/10, 11a/11, 11a/19, 12/3, 12/4a, 12/13, 12/14, 13/4, 13/12, 13/14, 13/15, 14/13, 14/15, 14/15, 14/16, 16/14, 16/15, 16/17, 17/14, 17/15, 17/16, 18/6, 18/8, 19/10, 18/11a; NOESY correlation (H/H) 3/11a, 3/12, 4a/8, 9/18, 11a/19, 14/17, 18/19; FABMS *m/z* 335 $[M+H]^+$; EIMS *m/z* 316 $[M-H_2O]^+$; HREIMS *m/z* 316.2043 (calcd for $C_{20}H_{28}O_3$, 316.2038).

Isoxeniatriacetate (2): Colorless oil; $[\alpha]^{27}_D$ –196° (*c* 0.55, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3391, 1737, 1240 cm^{-1}; UV (MeOH) λ_{max} 244 nm (ε 29,000); ^1H and ^{13}C NMR spectra see Table 1; HMBC correlation (H/C) 3/1, 3/4, 3/4a, 3/12, 4a/3, 4a/4, 4a/5, 4a/6, 4a/11a, 4a/12, 6/4a, 6/5, 6/7, 6/8, 6/18, 8/6, 8/9, 8/18, 9/7, 9/8, 9/10, 10/8, 10/9, 10/11, 10/11a, 10/19, 11a/1, 11a/4, 11a/4a, 11a/10, 11a/11, 11a/19, 12/3, 12/4a, 12/13, 12/14, 13/4, 13/12, 13/14, 13/15, 14/13, 14/15, 14/15, 14/16, 16/14, 16/15, 16/17, 17/14, 17/15, 17/16, 18/6, 18/8, 19/10, 18/11a; NOESY correlation (H/H) 3/11a, 3/12, 4a/8, 9/18, 11a/19, 14/17, 18/19, EIMS *m/z* 462 $[M]^+$; HREIMS *m/z* 462.2599 (calcd for $C_{26}H_{38}O_7$, 462.2618).

(*R*)-MTPA ester of dihydroxeniolide-A (1). To a solution of dihydroxeniolide-A (**1**) (1.0 mg, 3.0 μmol) in $CHCl_3$ (0.2 mL) were added DMAP (1.0 mg) and (*R*)-MTPA-Cl (2.0 mg, 7.9 μmol). After stirring at rt for 12 h, the reaction mixture was diluted with EtOAc and washed with H_2O and saturated NaCl aqueous solution. The organic layer was dried over $MgSO_4$ and concentrated under reduced presser. The residue was purified by silica gel column chromatography (hexane-EtOAc = 2 : 3) to give (*R*)-MTPA ester (1.0 mg, 61 %) as a colorless oil: $[\alpha]^{25}_D$ –21.7° (*c* 0.12, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3550, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.54 (2H, m), 7.41 (3H, m), 5.89 (1H, br t, *J* = 6.5 Hz), 5.61 (1H, dt, *J* = 15.5, 7.3 Hz), 5.50 (1H, dd, *J* = 15.5, 8.2 Hz), 5.29 (1H, d, *J* = 7.1 Hz), 4.76 (1H, s), 4.53

(1H, s), 4.17 (1H, dd, *J* = 11.5, 3.7 Hz), 4.01 (1H, dd, *J* = 11.5, 2.5 Hz), 3.59 (3H, s), 2.86 (1H, dd, *J* = 9.9, 8.2 Hz), 2.45 (1H, dd, *J* = 14.9, 5.9 Hz), 2.39 (1H, dd, *J* = 14.9, 1.5 Hz), 2.26 (2H, d, *J* = 7.1 Hz), 2.21 (1H, dt, *J* = 12.6, 2.9 Hz), 2.07 (1H, dt, *J* = 3.9, 12.6 Hz), 1.90 (1H, m), 1.79 (1H, m), 1.77 (3H, s), 1.74 (1H, m), 1.46 (1H, m), 1.24 (3H, s), 1.21 (3H, s); EIMS *m/z* 492 $[M\text{-}C_3H_6O]^+$; HREIMS *m/z* 492.2119 (calcd for $C_{27}H_{31}O_5F_3$, 492.2124).

(*S*)-MTPA ester of dihydroxeniolide-A (1). To a solution of dihydroxeniolide-A (**1**) (1.0 mg, 3.0 μmol) in $CHCl_3$ (0.2 mL) were added DMAP (1.0 mg) and (*S*)-MTPA-Cl (2.0 mg, 7.9 μmol). After stirring at rt for 12 h, the reaction mixture was diluted with EtOAc and washed with H_2O and saturated NaCl aqueous solution. The organic layer was dried over $MgSO_4$ and concentrated under reduced presser. The residue was purified by silica gel column chromatography (hexane-EtOAc = 2 : 3) to give (*S*)-MTPA ester (1.0 mg, 61 %) as a colorless oil: $[\alpha]^{25}_D$ –103° (*c* 0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3550, 1740 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.54 (2H, m), 7.42 (3H, m), 5.87 (1H, m), 5.61 (1H, dt, *J* = 15.5, 7.1 Hz), 5.52 (1H, dd, *J* = 15.5, 8.1 Hz), 5.20 (1H, d, *J* = 8.1 Hz), 4.86 (1H, s), 4.85 (1H, s), 4.18 (1H, dd, *J* = 11.5, 3.5 Hz), 4.04 (1H, dd, *J* = 11.5, 2.6 Hz), 3.53 (3H, s), 2.87 (1H, dd, *J* = 9.7, 8.1 Hz), 2.51 (1H, s), 2.50 (1H, s), 2.27 (2H, d, *J* = 7.1 Hz), 2.20 (1H, dt, *J* = 12.7, 3.2 Hz), 2.06 (1H, dt, *J* = 4.3, 12.7 Hz), 1.90 (1H, dt, *J* = 14.1, 3.6 Hz), 1.80 (1H, m), 1.77 (1H, m), 1.76 (3H, s), 1.55 (1H, m), 1.24 (3H, s), 1.21 (3H, s); EIMS *m/z* 550 $[M]^+$; HREIMS *m/z* 550.2558 (calcd for $C_{30}H_{37}O_6F_3$, 550.2542).

Photoisomerization of xeniolide-A (3) to isoxeniolide-A (4). A solution of xeniolide-A (**3**) (45.0 mg, 136 μmol) in benzene (20 mL) was irradiated with a 100W high-presser mercury lamp at rt for 5 h. The reaction mixture was concentrated under reduce presser. The residue was purified by HPLC (hexane-EtOAc = 2 : 3) to give isoxeniolide-A[11] (**4**) (39.5 mg, 88 %) as colorless crystals: $[\alpha]^{20}_D$ +41.0° (*c* 0.40, MeOH); mp 170-172°C; IR ($CHCl_3$) ν_{max} 3460, 1725, 1640 cm^{-1}; UV (MeOH) λ_{max} 263 nm (ε 16,100); ^1H NMR ($CDCl_3$, 400 MHz) δ 6.85 (1H, dd, *J* = 15.5, 11.1 Hz), 6.36 (1H, d, *J* = 11.1 Hz), 6.07 (1H, d, *J* = 15.5 Hz), 5.21 (1H, d, *J* = 7.3 Hz), 5.08 (1H, s), 4.96 (1H, s), 4.77 (1H, m), 4.08 (1H, dd, *J* = 11.4, 5.9 Hz), 3.63 (1H, dd, *J* = 12.3, 11.4 Hz), 2.60 (1H, m), 2.46 (1H, dd, *J* = 13.7, 6.1 Hz), 2.39 (1H, d, *J* = 13.7 Hz), 2.19 (2H, m), 2.01 (1H, m), 1.70 (3H, s), 1.64 (2H, m), 1.37 (3H, s), 1.37 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0 (s), 147.8 (s), 147.8 (s), 136.0 (d), 132.7 (s), 132.6 (s), 130.6 (d), 122.4 (d), 114.8 (t), 71.0 (t), 70.8 (s), 67.0 (d), 50.9 (d), 49.9 (d), 45.5 (t), 39.8 (t), 37.7 (t), 29.4 (q), 29.3 (q), 17.3 (q); EIMS *m/z* 273 $[M\text{-}C(CH_3)_2OH]^+$; HREIMS *m/z* 273.1465 (calcd for $C_{17}H_{21}O_3$, 273.1491).

DIBALH reduction of isoxeniolide-A (4) to tetraol (5). To a cold (-78°C) solution of isoxeniolide-A (**4**) (18.0 mg, 54 μmol) in THF (2.0 mL) was added DIBALH (600 μL, 558 μmol, 0.93M in hexane). The mixture was stirred for 10 min, treated with MeOH (0.1 mL), diluted with Et_2O, treated with saturated aqueous NaCl solution and stirred at rt for 2 h. The organic layer was dried over $MgSO_4$ and

concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane-acetone = 1 : 2) to afford tetraol (**5**) (10.0 mg, 55 %) as a colorless oil: $[\alpha]^{27}_{D}$ –184° (*c* 0.90, MeOH); IR ($CHCl_3$) ν_{max} 3430, 1635 cm^{-1}; UV (MeOH) λ_{max} 243 nm (ε 19,700); ^1H NMR ($CDCl_3$, 400 MHz) δ 6.56 (1H, dd, *J* = 15.2, 11.0 Hz), 5.96 (1H, d, *J* = 11.0 Hz), 5.80 (1H, d, *J* = 15.2 Hz), 5.29 (1H, d, *J* = 9.9 Hz), 5.01 (1H, s), 4.94 (1H, s), 4.62 (1H, dt, *J* = 5.4, 9.9 Hz), 4.25(2H, m), 3.49 (2H, m), 2.58 (1H, dd, *J* = 12.6, 5.1 Hz), 2.38 (1H, m), 2.19 (2H, m), 2.03 (1H, m), 1.95 (1H, m), 1.89 (1H, m), 1.63 (3H, s), 1.45 (2H, m), 1.34 (3H, s), 1.34 (3H, s); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.6 (d), 144.2 (s), 141.9 (s), 136.2 (s), 128.5 (d), 128.1 (d), 122.0 (d), 119.1 (t), 70.9 (s), 70.4 (d), 63.8 (t), 59.5 (t), 56.9 (d), 56.9 (d), 40.6 (t), 39.9 (t), 33.8 (t), 30.0 (q), 29.7 (q), 19.2 (q); EIMS *m/z* 287 $[M\text{-}H_2O\text{-}CH_2OH]^+$.

Acetylation of tetraol 5 to isoxeniatriacetate (2). To a solution of tetraol (**5**) (1.8 mg, 5.0 μmol) in pyridine (200 μL) was added acetic anhydride (200 μL), followed by stirring at rt for 15 min. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (hexane-EtOAc = 2 : 1) to give isoxeniatriacetate (**2**) (1.0 mg, 43 %) as a colorless oil: $[\alpha]^{22}_{D}$ –178° (*c* 0.09,$CHCl_3$).

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