Modiolides A and B, Two New 10-Membered Macrolides from a Marine-Derived Fungus

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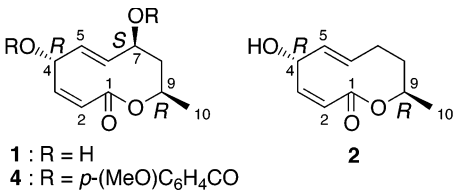
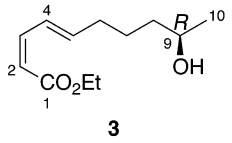
Two new 10-membered macrolides, modiolides A (**1**) and B (**2**), and a new linear pentaketide, modiolin (**3**), were isolated from the cultured broth of a fungus *Paraphaeosphaeria* sp. (N-119), which was separated from a marine horse mussel, and the structures were elucidated by spectroscopic data.

Marine-derived fungi have proven to be a rich source of structurally interesting and biologically active secondary metabolites.[1] In our search for new metabolites from marine-derived fungi,[2] two new 10-membered macrolides, modiolides A (**1**) and B (**2**), and a new related linear pentaketide, modiolin (**3**), were isolated from the cultured broth of the fungus *Paraphaeosphaeria* sp., which was separated from a marine horse mussel. In this paper we describe the isolation and structure elucidation of **1**−**3**.

The fungus *Paraphaeosphaeria* sp. (strain N-119) was separated from the horse mussel *Modiolus auriculatus* collected at Hedo Cape, Okinawa Island, and grown in PMG liquid medium containing seawater for 14 days at 25 °C. The supernatant of the culture broth (1 L) was extracted with EtOAc, and the EtOAc-soluble portions were subjected to silica gel column chromatography and then C_{18} HPLC to afford modiolides A (**1**, 1.1 mg) and B (**2**, 1.6 mg) and modiolin (**3**, 5 mg).





Modiolide A (**1**) showed the molecular ion peak at *m*/*z* 198 in the EIMS, and the molecular formula was revealed to be $C_{10}H_{14}O_4$ by HREIMS. IR absorption bands at 3292 and 1716 cm^{-1} were attributed to OH and carbonyl group(s), respectively. ^1H and ^{13}C NMR data (Table 1) disclosed the existence of an ester carbonyl (δ_C 170.9), four sp^2 methines (δ_C 139.4, 138.7, 131.8, and 123.7), three oxymethines (δ_C 73.6, 73.0, and 70.9), one sp^3 methylene (δ_C 44.7), and one methyl group (δ_C 22.4). Since three out of four unsaturations were accounted for, compound **1** was inferred to contain one ring. The $^1H-^1H$ COSY and HMQC spectra revealed connectivities from C-2 to C-10 (Figure 1). The HMBC correlation from H-2 to C-1 suggested that the ester carbonyl group was attached to C-2. The relatively lower-field resonance of H-9 (δ_H 5.25) suggested that C-9 was involved in an ester linkage to C-1. The existence of two hydroxyl groups at C-4 and C-7 was determined by a lower-field shift of H-4 and H-7 (δ_H 5.44 2H, m) by esterification with *p*-methoxycinnamoyl chloride (vide infra). This observation supported that **1** was a 10-membered macrolide. Geometries of two disubstituted olefins at C-2−C-3 and C-5−C-6 were assigned as *Z* and *E*, respectively, by $^1H-^1H$ coupling constants [*J*(H-2/H-3), 12.3 Hz; *J*(H-5/H-6), 15.8 Hz] and the NOESY correlation for H-2/H-3. Thus, the gross structure of modiolide A was elucidated to be **1**.

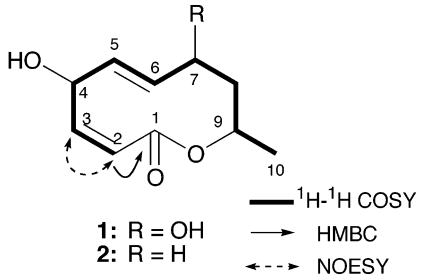


Figure 1. Selected 2D NMR correlations for modiolides A (**1**) and B (**2**).

The relative stereochemistry of **1** was deduced from $^1H-^1H$ coupling constants and NOESY data (Figure 2). A 1,3-*syn*-relation for 7-OH and C-10 was deduced from *J*(H-7/H-8α) and *J*(H-8α/H-9) (both 11.4 Hz) values and the NOESY correlation for H-7/H-9. On the other hand, a 1,4-*anti*-relation for OH-4 and OH-7 through the double bond at C-5−C-6 was indicated by NOESY correlations for H-4/H-6, H-5/H-7, and H-6/H-8α. To determine the absolute configurations at C-4 and C-7, the exciton chirality method[3] using a *p*-methoxycinnamoyl group was applied. Treatment of **1** with *p*-methoxycinnamoyl chloride afforded the 4,7-bis-*O*-*p*-methoxycinnamoyl ester (**4**). The CD spectrum of **4** disclosed a positive first (λ_{ext} 324 nm, $\Delta\epsilon$ +18) and a negative second Cotton effect (λ_{ext} 289 nm, $\Delta\epsilon$ −8.0), indicating 4*R*- and 7*S*-configurations. Therefore, the absolute configuration of modiolide A (**1**) was elucidated to be 4*R*, 7*S*, and 9*R*.

The molecular formula, $C_{10}H_{14}O_3$, of modiolide B (**2**) was established by the molecular ion peak at *m*/*z* 182.0994 in

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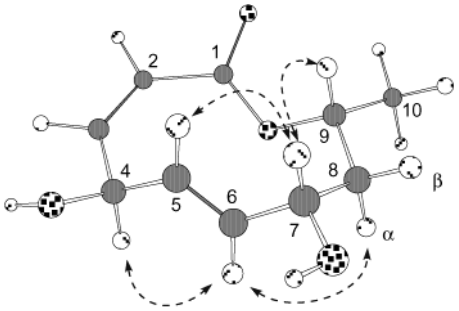
Table 1. ^{1}H and ^{13}C NMR Data of Modiolides A (**1**) and B (**2**) in CD_3OD

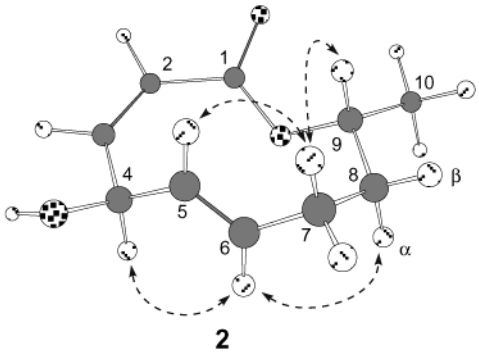
	1					**2**				
position	δ_H		J, Hz	δ_C		δ_H		J, Hz	δ_C	
1				170.9	s				170.8	s
2	5.85	dd	1.5, 12.3	123.7	d	5.85	dd	1.4, 12.3	123.0	d
3	5.83	dd	3.5, 12.3	138.7	d	5.83	dd	2.9, 12.3	138.0	d
4	4.68	br dd	3.5, 7.3	73.0	d	4.67	br dd	2.9, 8.2	72.6	d
5	5.61	dd	7.3, 15.8	131.8	d	5.45	ddd	1.5, 8.2, 15.2	130.2	d
6	5.56	dd	7.5, 15.8	139.4	d	5.69	ddd	3.5, 11.0, 15.2	136.2	d
7	4.12	ddd	2.5, 7.5, 11.4	73.6	d	(α) 2.37	dddd	2.4, 3.5, 5.3, 13.5	32.0	t
						(β) 2.15	ddt	2.6, 13.5, 11.0		
8	(α) 1.71	dt	14.0, 11.4	44.7	t	(α) 1.65	ddt	2.4, 14.7, 11.0	34.9	t
	(β) 1.87	dt	14.0, 2.5			(β) 1.71	ddt	5.3, 14.7, 2.6		
9	5.25	ddq	2.5, 11.4, 6.7	70.9	d	5.61	ddq	2.6, 11.0, 6.7	73.7	t
10	1.22[a]	d	6.7	22.4	q	1.22[a]	d	6.7	21.7	q

[a] 3H.



1

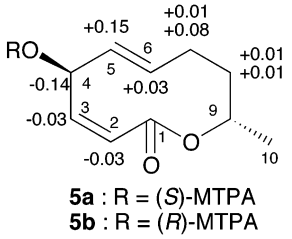
Figure 2. NOESY correlations and relative stereochemistry for modiolide A (**1**). NOESY correlations are shown by dotted arrows. J in Hz (H/H): H-2/H-3, 12.3; H-4/H-5, 7.3; H-5/H-6, 15.8; H-6/H-7, 7.5; H-7/H-8α, 11.4; H-7/H-8β, 2.5; H-8α/H-9, 11.4; H-8β/H-9, 2.5.



2

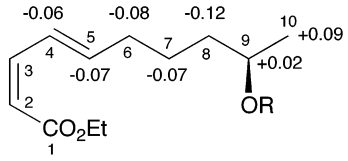
Figure 3. NOESY correlations and relative stereochemistry for modiolide B (**2**). NOESY correlations are shown by dotted arrows. J in Hz (H/H): H-2/H-3, 12.3; H-4/H-5, 8.2; H-5/H-6, 15.2; H-6/H-7α, 3.5; H-6/H-7β, 11.0; H-7α/H-8α, 2.4; H-7α/H-8β, 5.3; H-7β/H-8α, 11.0; H-7β/H-8β, 2.6; H-8α/H-9, 11.0; H-8β/H-9, 2.6.

the HREIMS. ^{1}H and ^{13}C NMR data (Table 1) of **2** disclosed the presence of one ester carbonyl, two disubstituted olefins, which were assigned as *Z* (C-2−C-3) and *E* (C-5−C-6), two oxymethines, two methylenes, and one methyl group. Analysis of ^{1}H−^{1}H COSY, HMQC, and HMBC spectra revealed that **2** was the 7-deoxy form of modiolide A (**1**) (Figure 1). Since the lower-field shift of H-4 was observed by esterification of **2**, it revealed that a hydroxyl group was attached to C-4 (vide infra). Although H-9 did not show the HMBC correlation for C-1, the relatively lower-field resonance (δ_H 5.61) suggested that C-9 was involved in an ester linkage to C-1. The relative stereochemistry between H-4 and H-9 was assigned as an *anti*-relation on the basis of NOESY correlations and ^{1}H−^{1}H coupling constants as shown in Figure 3. The 4*R*-configuration was deduced from a modified Mosher's method[4] using the (*S*)- and (*R*)-MTPA esters (**5a** and **5b**, respectively) of **2** (Figure 4), and the 9*R*-stereochemistry was inferred through relative stereochemistry.



5a : R = (*S*)-MTPA
5b : R = (*R*)-MTPA

Figure 4. $\Delta\delta$ values [$\Delta\delta$ (in ppm) = $\delta_S - \delta_R$] obtained for (*S*)- and (*R*)-MTPA esters (**5a** and **5b**, respectively) of modiolide B (**2**).



6a : R = (*S*)-MTPA
6b : R = (*R*)-MTPA

Figure 5. $\Delta\delta$ values [$\Delta\delta$ (in ppm) = $\delta_S - \delta_R$] obtained for (*S*)- and (*R*)-MTPA esters (**6a** and **6b**, respectively) of modiolin (**3**).

The molecular formula of modiolin (**3**) was revealed to be $C_{12}H_{20}O_3$ by HREIMS. IR (1716 cm^{-1}) and UV absorptions (260 nm) indicated the presence of an unsaturated ester chromophore. ^{1}H and ^{13}C NMR data suggested the presence of an ester carbonyl, two disubstituted double bonds, an oxymethine, an oxymethylene, three methylenes, and two methyls. Analysis of ^{1}H−^{1}H COSY and HMQC spectra disclosed connectivities from C-2 to C-10 and the exsistence of an ethoxy group. HMBC correlations from H-2 and the oxymethylene protons (δ_H 4.13; 2H) to C-1 indicated that the ethoxy carbonyl group was attached to C-2. Thus, the gross structure of **3** was assigned as ethyl (2*Z*,4*E*)-9-hydroxydecan-2,4-dienoate. The absolute configuration at C-9 was determined to be *R* on the basis of a modified Mosher's method using the (*S*)- and (*R*)-MTPA esters (**6a** and **6b**, respectively) of **3** (Figure 5).

Although 10-membered macrolides such as diplodialides A−D and pyrenolides A−C have been isolated from the terrestrial fungi *Diplodia pinea*,[5,6] *Pyrenophora teres*,[7,8] and *Cephalosporium ahidicola*,[9−12] modiolides A (**1**) and B (**2**) are the first 10-membered macrolides from a marine-derived fungus. Modiolides A (**1**) and B (**2**) showed antibacterial activity against *Micrococcus luteus* (MIC value 16.7 μg/mL) and antifungal activity against *Neurospora crassa* (MIC value 33.3 μg/mL).

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP-1000 polarimeter. IR and UV

spectra were recorded on a JASCO FT/IR-5300 and a Shimadzu UV-1600PC spectrophotometer, respectively. CD spectra were measured on a JASCO J-720 spectropolarimeter. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-600 spectrometer using 2.5 mm micro cells for CD_3OD or $CDCl_3$ (Shigemi Co., Ltd.). ^{1}H−^{1}H coupling constants were based on the resolution-enhanced ^{1}H NMR spectra. EIMS spectra were recorded on a JEOL FABmate spectrometer at 70 eV. ESI mass spectra were recorded on a Shimadzu LCMS QP-8000 and a JEOL 700TZ spectrometer. FAB mass spectra were obtained on a JEOL HX-110 spectrometer using nitrobenzyl alcohol as a matrix.

Fungal Material and Fermentation. The fungus *Paraphaeosphaeria* sp. (N119) was separated from the horse mussel *Modiolus auriculatus* (family, Mytilidae; order, Mytiloida), which was collected at Hedo Cape, Okinawa Island. DNA of the fungus was extracted using ISOPLANT II kit (Nippon Gene Co. Ltd. Tokyo, Japan). 18S rDNA and the ITS region including the 5.8S rDNA were amplified by PCR using the primer pairs proposed by White et al.[13] and sequenced using an ABI PRISM 377-18 DNA sequencer (Applied Biosystems, Foster City, CA). The DNA sequence was compared with those in the databases using BLAST SEARCH.[14] The strain N119 was assigned to the anamorph state of *Paraphaeosphaeria* sp. N119 on the basis of the fact that the most relative molecules were 18S rDNA of *Paraphaeosphaeria michotii* (accession no. AF250817) and ITS region of *Paraphaeosphaeria pilleata* (accession no. AF250821). The sequence data of the strain N119 have been submitted to the DDBJ/EMBL/GenBank under accession no. AB096264. Subcultures of the organism are deposited at the Graduate School of Pharmaceutical Sciences, Hokkaido University. The fungus was grown in PMG seawater medium (peptone, 0.05%; D-glucose, 1%; malt extract, 1%; pH 7.5) for 14 days at 25 °C. The cultured broth (1 L) was filtered.

Extraction and Separation. The mycelium of the cultured broth was extracted with EtOAc (1 L × 2). The EtOAc-soluble portions (108 mg) were subjected to silica gel column chromatography ($CHCl_3$/MeOH, 99:1 → 95:5). The fraction eluted by $CHCl_3$/MeOH (95:5) was separated by C_{18} HPLC (YMC-Pack Hydrosphere C18, YMC Co., Ltd., 10 × 250 mm; flow rate 2.5 mL/min; UV detection at 220 nm; eluent MeOH/H_2O, 22:88) to give modiolide A (**1**, 1.1 mg, t_R 31 min). The fraction eluted by $CHCl_3$/MeOH (99:1 → 98:2) was separated by C_{18} HPLC (YMC-Pack Hydrosphere C18, 10 × 250 mm; flow rate 2.5 mL/min; UV detection at 270 nm; eluent MeOH/H_2O, 30:70) to give modiolide B (**2**, 1.6 mg, t_R 18 min) and modiolin (**3**, 5.0 mg, t_R 21 min).

Modiolide A (1): colorless oil; $[\alpha]^{18}_D$ +42° (*c* 0.25, MeOH); UV (MeOH) λ_{max} 204 nm (ϵ 6400); IR (KBr) ν_{max} 3292 and 1716 cm^{-1}; ^{1}H and ^{13}C NMR (Table 1); EIMS *m*/*z* 180 $(M - H_2O)^+$ and 198 (M^+); HREIMS *m*/*z* 198.0892 (M^+, calcd for $C_{10}H_{14}O_4$, 198.0891).

Modiolide B (2): colorless oil; UV (MeOH) λ_{max} 204 nm (ϵ 6400); IR (KBr) ν_{max} 3292 and 1716 cm^{-1}; ^{1}H and ^{13}C NMR (Table 1); EIMS *m*/*z* 164 $(M - H_2O)^+$ and 182 (M^+); HREIMS *m*/*z* 182.0944 (M^+, calcd for $C_{10}H_{14}O_4$, 182.0943).

Modiolin (3): colorless oil; UV (MeOH) λ_{max} 260 nm (ϵ 17500); IR (KBr) ν_{max} 3422 and 1716 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.12 (3H, d, J = 6.7 Hz, H_3-10), 1.24 (3H, t, J = 7.2 Hz, OCH_2CH_3), 1.35−1.50 (3H, m, H-7 and H_2-8),1.55 (1H, m, H-7), 2.19 (1H, m, H_2-6), 3.78 (1H, m, H-9), 4.13 (2H, q, J = 7.2 Hz, OCH_2CH_3), 5.26 (1H, d, J = 11.3 Hz, H-2), 6.03 (1H, dt, J = 14.6 and 7.0 Hz, H-5), 6.52 (1H, t, J = 11.0 Hz, H-3), and 7.36 (1H, dd, J = 11.0 and 14.6 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 166.6 (s, C-1), 145.2 (d, C-3), 145.0 (d, C-5), 127.3 (d, C-4), 115.8 (d, C-2), 68.0 (d, C-9), 59.9 (t, OCH_2CH_3), 38.8 (t, C-8), 32.9 (t, C-6), 25.0 (t, C-7), 23.6 (q, C-10), and 14.4 (q, OCH_2CH_3); EIMS *m*/*z* 194 $(M - H_2O)^+$ and 212 (M^+); HREIMS *m*/*z* 212.1415 (M^+, calcd for $C_{12}H_{20}O_3$, 212.1412).

4,7-Bis-*O*-*p*-methoxycinnamoyl Ester (4) of 1. To a pyridine solution (50 μL) of modiolide A (**1**, 0.1 mg) was added 4-(dimethylamino)pyridine (50 μg) and then *p*-methoxycinnanmoyl chloride (1.2 mg) at room temperature, and stirring was continued for 5 h. After addition of phosphate buffer (pH 6.85, 50 μL), the reaction mixture was extracted with $CHCl_3$ (100 μL × 3), and then the organic layer was evaporated in vacuo. The residue was subjected to C_{18} HPLC (YMC-Pack J'sphere ODS-H80, 4.6 × 250 mm; flow rate 1.0 mL/min; UV detection at 310 nm; eluent CH_3CN/H_2O, 70:30) to afford the 4,7-bis-*O*-*p*-methoxycinnamate (**4**, 0.1 mg, t_R 19.6 min) of **1** as a colorless oil: UV (MeOH) λ_{max} 320 (ϵ 32000), 300 (sh), and 220 nm (sh); CD (MeOH) λ_{ext} 324 ($\Delta\epsilon$ +18) 299 (0), and 289 nm (−8.0); ^{1}H NMR ($CDCl_3$) δ 1.29 (3H, d, J = 6.7 Hz, H_3-10), 1.94 (1H, dt, 14.0 and 11.4 Hz, H-8α), 2.06 (1H, brd, J = 14.0 Hz, H-8β), 3.84 (6H, s, OCH_3), 5.44 (2H, m, H-4 and H-7), 5.84−6.04 (5H, m, H-2, H-3, H-5, H-6, and H-9), 6.25 (1H, d, J = 15.5 Hz, H-2′), 6.27 (1H, d, J = 15.5 Hz, H-2′), 6.90 (4H, d, J = 8.9 Hz, H_2-6′ and H_2-8′), 7.43 (2H, d, J = 8.9 Hz, H_2-5′ and H_2-9′), 7.63 (1H, d, J = 15.9 Hz, H-3′), and 7.65 (1H, d, J = 15.9 Hz, H-3′); ESIMS *m*/*z* 541 $(M + Na)^+$; HRESIMS *m*/*z* 541.1874 [$(M + Na)^+$, calcd for $C_{30}H_{30}O_8Na$, 541.1839].

4-(*S*)-MTPA Ester (5a) of 2. To a CH_2Cl_2 solution (50 μL) of modiolide B (**2**, 0.1 mg) was added 4-(dimethylamino)-pyridine (50 μg), triethylamine (5 μL), and (*R*)-(−)-MTPACl (3 μL) at room temperature, and stirring was continued for 14 h. *N*,*N*-Dimethyl-1,3-propanediamine (3 μL) was added, and the reaction mixture was stirred for 10 min. After addition of phosphate buffer (pH 6.85, 50 μL), the reaction mixture was evaporated in vacuo. The residue was subjected to a SiO_2 column (hexane/acetone, 8:1) and then C_{18} HPLC (YMC-Pack J'sphere ODS-H80, 4.6 × 250 mm; flow rate 1.0 mL/min; UV detection at 230 nm; eluent CH_3CN/H_2O, 75:25) to afford the 4-(*S*)-MTPA ester (**5a**, 0.1 mg, t_R 14.4 min) of **2**. **5a**: colorless oil; ^{1}H NMR (CD_3OD) δ 1.24 (3H, d, J = 6.7 Hz, H_3-10), 1.72 (1H, m, H-8α), 1.78 (1H, m, H-8β), 2.26 (1H, m, H-7β), 2.48 (1H, m, H-7α), 3.57 (3H, s, OCH_3), 5.36 (1H, m, H-9), 5.57 (1H, dd, J = 8.2 and 15.2 Hz, H-5), 5.77 (1H, dd, J = 2.9 and 8.2 Hz, H-4), 6.02 (1H, ddd, J = 3.4, 11.0, and 15.2 Hz, H-6), 6.07 (1H, d, J = 12.3 Hz, H-2), 6.10 (1H, brd, J = 12.3 Hz, H-3), 7.49 (3H, m, Ph), and 7.54 (2H, m, Ph); FABMS *m*/*z* 421 $(M + Na)^+$; HRFABMS *m*/*z* 421.1252 [$(M + Na)^+$, calcd for $C_{20}H_{21}O_5F_3Na$, 421.1239].

4-(*R*)-MTPA Ester (5b) of 2. Modiolide B (**2**, 0.1 mg) was treated with (*S*)-(+)-MTPACl (3 μL) by the same procedure as described above to afford the (*R*)-MTPA ester (**5b**, 0.1 mg) of **2**. **5b**: colorless oil; ^{1}H NMR (CD_3OD) δ 1.24 (3H, d, J = 6.7 Hz, H_3-10), 1.72 (1H, m, H-8α), 1.78 (1H, m, H-8β), 2.20 (1H, m, H-7β), 2.45 (1H, m, H-7α), 3.58 (3H, s, OCH_3), 5.32 (1H, m, H-9), 5.40 (1H, dd, J = 8.2 and 15.2 Hz, H-5), 5.88 (1H, dd, J = 2.9 and 8.2 Hz, H-4), 5.97 (1H, ddd, J = 3.4, 11.0, and 15.2 Hz, H-6), 6.08 (1H, brd, J = 12.3 Hz, H-3), 6.11 (1H, d, J = 12.3 Hz, H-2), 7.49 (3H, m, Ph), and 7.54 (2H, m, Ph); FABMS *m*/*z* 421 $(M + Na)^+$; HRFABMS *m*/*z* 421.1242 [$(M + Na)^+$, calcd for $C_{20}H_{21}O_5F_3Na$, 421.1239].

9-(*S*)-MTPA Ester (6a) of 3. To a CH_2Cl_2 solution (50 μL) of modiolin (**3**, 0.1 mg) was added 4-(dimethylamino)pyridine (50 μg), triethylamine (5 μL), and (*R*)-(−)-MTPACl (3 μL) at room temperature, and stirring was continued for 14 h. *N*,*N*-Dimethyl-1,3-propanediamine (3 μL) was added, and the reaction mixture was stirred for 10 min. After addition of phosphate buffer (pH 6.85, 50 μL), the reaction mixture was evaporated in vacuo. The residue was subjected to a SiO_2 column (hexane/acetone, 8:1) and then C_{18} HPLC (YMC-Pack J'sphere ODS-H80, 4.6 × 250 mm; flow rate 1.0 mL/min; UV detection at 230 nm; eluent CH_3CN/H_2O, 80:20) to afford the 4-(*S*)-MTPA ester (**6a**, 0.1 mg, t_R 15.4 min) of **3**. **6a**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.29 (3H, t, J = 7.0 Hz, OCH_2CH_3), 1.30 (1H, H-8α), 1.34 (3H, d, J = 6.7 Hz, H_3-10), 1.36 (2H, m, H-8β), 1.54 (1H, m, H-7β), 1.63 (1H, m, H-7α), 2.13 (2H, m, H_2-6), 3.57 (3H, s, OCH_3), 4.18 (2H, q, J = 7.0 Hz, OCH_2CH_3), 5.16 (1H, m, H-9), 5.57 (1H, d, J = 11.3 Hz, H-2), 5.90 (1H, dd, J = 8.2 and 15.2 Hz, H-5), 6.51 (1H, t, J = 11.0 Hz, H-3), 7.32 (1H, dd, J = 11.0 and 14.6 Hz, H-4), 7.39 (3H, m, Ph), and 7.53 (2H, m, Ph); FABMS *m*/*z* 429 $(M + H)^+$; HRFABMS *m*/*z* 429.1877 [$(M + H)^+$, calcd for $C_{22}H_{28}O_5F_3$, 429.1889].

9-(*R*)-MTPA Ester (6b) of 3. Modiolin (**3**, 0.1 mg) was treated with (*S*)-(+)-MTPACl (3 μL) by the same procedure as described above to afford the (*R*)-MTPA ester (**6b**, 0.1 mg) of

3. **6b**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.26 (3H, d, J = 6.7 Hz, H_3-10), 1.29 (3H, t, J = 7.0 Hz, OCH_2CH_3), 1.46 (1H, H-8α), 1.49 (2H, m, H-8β), 1.58 (1H, m, H-7β), 1.70 (1H, m, H-7α), 2.21 (2H, m, H_2-6), 3.54 (3H, s, OCH_3), 4.19 (2H, q, J = 7.0 Hz, OCH_2CH_3), 5.14 (1H, m, H-9), 5.58 (1H, d, J = 11.3 Hz, H-2), 5.97 (1H, dd, J = 8.2 and 15.2 Hz, H-5), 6.53 (1H, t, J = 11.0 Hz, H-3), 7.35 (1H, dd, J = 11.0 and 14.6 Hz, H-4), 7.39 (3H, m, Ph), and 7.53 (2H, m, Ph); FABMS m/z 429 $(M + H)^+$; HRFABMS m/z 429.1879 [$(M + H)^+$, calcd for $C_{22}H_{28}O_5F_3$, 429.1889].

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