Isolation and Structures of Antibacterial Binaphtho-α-pyrones, Talaroderxines A and B, from *Talaromyces derxii*[1)]

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New compounds designated talaroderxines A (1) and B (2) were isolated from a new heterothallic ascomycetous fungus, *Talaromyces derxii*, cultivated on rice. The structures of 1a and 1b were elucidated by means of spectroscopic examination and chemical reactions. Talaroderxines A (1a) and B (1b) are atropisomers of a 6,6′-binaphtho-α-pyrone derivative, and have strong antibacterial activity against *Bacillus subtilis*.

Keywords *Talaromyces derxii*; 6,6′-binaphtho-α-pyrone; talaroderxine A; talaroderxine B; viriditoxin; atropisomer; antibacterial activity

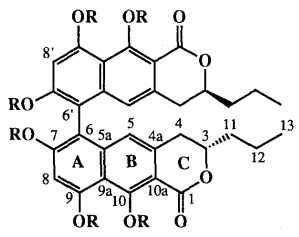
The ascomycetous fungus, *Talaromyces derxii* TAKADA *et* UDAGAWA (anamorph: *Penicillium derxii* TAKADA *et* UDAGAWA) isolated from cultivated soil at Kurashiki, western Japan, is the first heterothallic teleomorph with a *Penicillium* state to have been found.[2)] Recently three new derivatives of prenylated *p*-hydroxybenzoic acid[3)] were isolated from the extract of the filtrate of *T. derxii*, strain NHL 2982 (mating type a), cultivated in the Czapek medium supplemented with 0.2% yeast extract. When *T. derxii* was cultivated on rice, the infected rice became green, and some of the green pigments could be extracted with dichloromethane. In the course of the separation of the green pigments, we reported[1)] the structural elucidation of dehydroisopenicillide, a new minor metabolite, and the absolute configuration of penicillide, both isolated from the extract of *T. derxii*, strain NHL 2981 (mating type A). The antibacterial activity against *Bacillus subtilis* COHN shown by the above extract of *T. derxii* cultivated on rice prompted us to make a further investigation. As one of the main components, talaroderxine (**1**), which has strong antibacterial activity, was obtained. Sixteen carbon-13 nuclear magnetic resonance (^{13}C-NMR) signals (Table I) were observed for **1**, but some of these signals showed doubling. So **1** was considered to be a mixture or an equilibrium mixture of two isomers, but attempts to separate them were unsuccessful. On acetylation, **1** afforded two isomeric hexaacetates (**2a** and **2b**), which were separated by repeated low pressure liquid chromatography (LPLC). Methanolysis of **2a** and **2b** gave the isomers, designated talaroderxines A (**1a**) and B (**1b**), respectively. Therefore talaroderxine (**1**) is a mixture of two isomers (**1a** and **1b**). We now report the structural elucidation of **1a** and **1b**.

The high-resolution mass spectrometry of talaroderxines A (**1a**) and B (**1b**) confirmed the molecular formulae as $C_{32}H_{30}O_{10}$. The proton nuclear magnetic resonance (^{1}H-NMR) spectra and the other spectral data of talaroderxines A (**1a**) and B (**1b**) were superimposable, but the isomers showed opposite circular dichroism (CD)

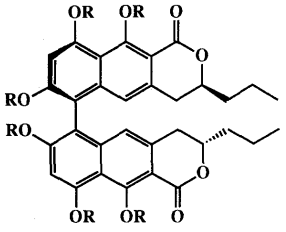
TABLE I. ^{13}C-NMR Data for Talaroderxines and Their Derivatives in $(CD_3)_2SO$

Carbon	1	2a	2b	3	4[a)]	5[a,b)]	6
1	170.72	162.62	162.53	169.92	170.5	169.8	161.59 161.62
3	79.13 79.18	79.28	79.24	75.69	76.0	75.8	76.69
4	32.29 32.34	35.17	35.22	31.71	33.8	32.7[c)]	33.82 33.93
4a	133.12	138.48	138.47	133.05	134.0	132.2	136.30 136.37
5	113.06	123.17	123.07	112.91	115.4	116.4	117.32
5a	139.77 139.82	138.94	138.85	138.71	140.3	140.6	138.59 138.65
6	107.70 107.75	117.43	117.41	109.35	100.9	101.8	109.81 109.84
7	158.89 159.00	149.76	149.71	160.16	157.6[c)]	158.6[d)]	158.00 158.12
8	101.73 101.76	119.60	119.06	98.09	99.1	99.7	95.65
9	157.35	150.85	150.85	158.34	161.7	162.8	158.91
9a	107.23 107.27	121.19	121.15	107.67	108.1[d)]	108.4[e)]	114.79
10	162.36	150.47	150.46	162.36	161.9[c)]	163.2[d)]	161.42 161.50
10a	98.53	121.72	121.77	98.84	99.4[d)]	99.1[e)]	112.62 112.75
11	36.04	37.86	37.75	38.67	20.3	39.4[c)]	36.02 36.05
12	17.42	19.20	19.25	169.92		170.7	17.45
13	13.56	14.51	14.48	51.57		52.2	13.62
7-OMe				55.86		55.5	55.94 55.98
7-OCO$\underline{CH_3}$		21.71[f)]	21.71[f)]				
7-O$\underline{C}$OCH$_3$		170.21[g)]	170.22[g)]				
9-OMe							56.32
9-OCO$\underline{CH_3}$		20.97[f)]	20.87[f)]				
9-O$\underline{C}$OCH$_3$		169.45[g)]	169.34[g)]				
10-OMe							62.63
10-OCO$\underline{CH_3}$		22.10[f)]	22.09[f)]				
10-O$\underline{C}$OCH$_3$		170.34[g)]	170.34[g)]				

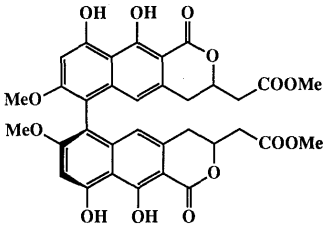
a) Data were taken from reference 7. *b*) The spectrum was measured in $CDCl_3$. *c*—*e*) The assignments were revised. *f*, *g*) The assignments may be reversed.



1 : R = H
6 : R = Me



1a : R = H
2a : R = Ac



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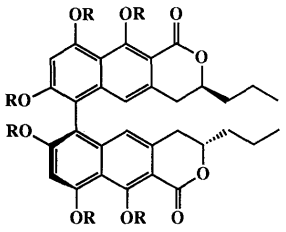
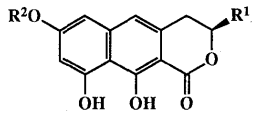
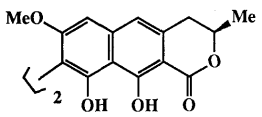


1b : R = H
2b : R = Ac



4 : R^1 = Me, R^2 = H
5 : R^1 = CH_2COOMe, R^2 = Me



7

Table II. CD Spectra of Talaroderxines and Their Derivatives in MeOH [$\Delta\varepsilon$ (nm)]

Compound	1st Cotton	2nd Cotton	Others	Configuration
1a	+103.6 (267)	−80.9 (246)	−6.5 (320)	*S*
1b	−92.7 (267)	+70.6 (246)	+7.1 (320)	*R*
2a	+139.7 (263)	−172.7 (239)	−14.2 (311)	*S*
2b	−138.2 (264)	+179.3 (240)	+13.7 (310)	*R*
3	−194.7 (275)	+174.0 (255)	+11.0 (324)	*R*
6	+11.1 (258)	−2.2 (243)	+11.6 (222), −2.6 (345)	

Table III. Antibacterial Activities of Metabolites Isolated from *T. derxii* and Viriditoxin against *B. subtilis*

Compound	Amount of metabolites (μg/disc)							
	50	25	10	5	1	0.5	0.25	0.1
Extract[a]	21[b]	20	15	12	±[c]	−[d]	−	−
1 (**1a**+**1b**)	20	20	20	20	11	9	±	−
2a	−	−	−	−	−	−	−	−
2b	−	−	−	−	−	−	−	−
3	21	20	20	19	16	13	±	−
6	−	−	−	−	−	−	−	−
Penicillide	−	−	−	−	−	−	−	−
Dehydroiso-penicillide	−	−	−	−	−	−	−	−

a) The CH_2Cl_2 extract of the rice infected with *T. derxii*. *b*) Diameter of inhibition circle (mm). *c*) Plus-minus (±) means that inhibition was unequivocal. *d*) Minus (−) means no inhibition.

curves. The spectral data of hexa-*O*-acetyltalaroderxines A (**2a**) and B (**2b**) are also closely similar to each other except the CD spectra. The above results indicated that **1a** and **2a** are atropisomers of **1b** and **2b**, respectively. Since only 22 carbon signals were observed in the ^{13}C-NMR spectra of **2a** and **2b**, they were considered to be symmetrical dimeric compounds.

The ^{1}H-NMR spectra of the skeleton and the ultraviolet (UV) spectra of **1a** and **1b** were similar to those of viriditoxin (**3**), which was isolated first from *Aspergillus viridinutans* Ducker *et* Thrower[4] and then as SC-28762 from *Paecilomyces variotii* Thom.,[5] and of 7-de-*O*-methylsemivioxanthin (**4**), isolated from *Penicillium janthinellum* Biorge,[6] and also of semiviriditoxin (**5**), isolated from *P. variotii*.[7] From the above facts, **1a** and **1b** were assumed to be atropisomers of a naphtho-α-pyrone dimer. The ^{1}H-NMR signals at δ 1.548 (2H), 1.675 (2H), 1.405 (4H), and 0.883 (6H) in **1a** and those at δ 1.601 (2H), 1.661 (2H), 1.399 (4H), and 0.876 (6H) in **1b** were assigned to the side chain *n*-propyl groups from the correlations in the ^{1}H–^{1}H shift correlation (COSY) spectra. Since correlation peaks were observed between the methine protons at C-3 (δ 4.552 in **1a** and δ 4.541 in **1b**) and the methylene protons of the propyl residues [δ 1.548 (1.675) in **1a** and 1.601 (1.661) in **1b**] in the COSY spectra of **1a** and **1b**, respectively, it was confirmed that the propyl group was attached to the naphtho-α-pyrone moiety at C-3. The methylene protons at C-4 were correlated to one [δ 6.219 (6.246)] of the aromatic protons in the COSY spectra. Therefore the above aromatic proton was located at C-5. The absorption at 1640 cm^{-1} in the infrared (IR) spectra of **1a** and **1b** suggested that the carbonyl group at C-1 of the naphtho-α-pyrone moiety was strongly hydrogen-bonded. The downfield D_2O-exchangeable proton signals at δ 13.350 in **1a** and δ 13.485 in **1b** were assigned to the hydroxyl proton attached at C-10.

Talaroderxine (**1**), the mixture of **1a** and **1b**, gave a hexamethyl ether (**6**) upon methylation with dimethyl sulfate. In order to confirm the substitution pattern of the aromatic ring A in **1a** and **1b**, the difference nuclear Overhauser enhancement (NOE) spectra of **6** in $CDCl_3$ were studied. When one of the aromatic protons (δ 6.796) was irradiated, 6.4% and 5.4% NOE's for the methoxy protons at δ 3.782 (3.822) and 4.123 were observed, while enhancements, 18.8% and 18.0% respectively, of the above aromatic proton were observed when the above methoxy protons were irradiated. No NOE was observed on the methoxy groups when the aromatic proton at C-5, which appeared at δ 6.520 (6.576), was irradiated. These results clearly showed that the aromatic proton at δ 6.796 is located at C-8, *i.e.*, *ortho* to two methoxy groups, and no methoxy group was located *peri* to the aromatic proton at C-5. Detailed analysis of the ^{1}H–^{13}C long-range shift-correlated spectrum of **6** also supported this structure. Thus, the structure of hexamethyltalaroderxine was determined as **6**, and consequently the structures of talaroderxines A (**1a**) and B (**1b**) were confirmed to be 7,9,10,7′,9′,10′-hexahydroxy-3,3′-dipropyl-6,6′-binaphtho-α-pyrone.

The chirality of the axis between the two naphtho-α-pyrone moieties in talaroderxines A (**1a**) and B (**1b**), and hexa-*O*-acetyltalaroderxines A (**2a**) and B (**2b**), was con-

firmed by the exciton chirality method.[8] The CD spectra of **1b** and **2b** exhibited strong negative first and positive second Cotton effects, like those of viriditoxin (**3**) (Table II). These are due to the coupling between the ^1B_b transitions of the two naphthalene chromophores, and this phenomenon shows that the long axes of the naphtho-α-pyrone moieties in **1b** and **2b** are twisted in a counterclockwise manner. Thus, the chirality of the 6,6′-axis in talaroderxine B (**1b**) and its acetate (**2b**) was found to be *R*. The CD spectra of **1a** and **2a** exhibited strong positive first and negative second Cotton effects, being antipodal to those of viriditoxin (**3**) (Table II). Therefore talaroderxine A (**1a**) and its acetate (**2a**) have *S*-configuration on the 6,6′-axis. Since the CD curves of talaroderxine hexamethyl ethers (**6**) (Table II) did not show strong Cotton effects at 260—270 nm and 240—250 nm, **6** should be the mixture of the atropisomers.

Thus, the only problem that remained was the stereochemistry at C-3. Talaroderxine (**1**) was ozonized in methanol at −60 °C[9] followed by oxidation with alkaline hydroperoxide, to afford (+)-3-hydroxyhexanoic acid, $[\alpha]_D$ +22.3° (chloroform), which was consistent with that of (*S*)-3-hydroxyhexanoic acid, $[\alpha]_D$ +24.4°.[10,11] The absolute configuration at C-3 in **1a** and **1b** was confirmed to be *S*. Therefore the absolute structures of talaroderxines A and B were determined to be as shown in **1a** and **1b**, respectively.

The extract of rice infected with *T. derxii* had antibacterial activity against *B. subtilis*. The antibacterial activities of the metabolites from *T. derxii* and their derivatives against *B. subtilis* are summarized in Table III. Only talaroderxine (**1**), the mixture of **1a** and **1b**, showed antibacterial activity, which was almost as strong as that of viriditoxin (**3**). Talaroderxine (**1**), in addition, has inhibitory activity toward 5-lipoxygenase. Its IC_{50} value was determined as 3.8×10^{-6} M.

Viriditoxin (**3**) and vioxanthin (**7**) were isolated from *Trichophyton violaceum* SABOURAUD,[12] *etc.*, as the fungal metabolites having binaphtho-α-pyrone structures. Whereas 3-methylbinaphtho-α-pyrones ever known like **7** are 8,8′-dimers, it is noteworthy that binaphtho-α-pyrones having a three-carbon residue at C-3, *i.e.*, talaroderxines A (**1a**) and B (**1b**), and viriditoxin (**3**), whose structure was revised recently,[13] are 6,6′-dimers.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotation was measured with a JASCO DIP-181 spectrometer. Electron impact ionization mass spectra (EI-MS) and fast-atom bombardment mass spectra (FAB-MS), using thioglycerol as a matrix, were taken with a JEOL JMS-D-300 spectrometer and a JEOL JMX-HS-110 spectrometer, respectively. UV and IR spectra were recorded on a Hitachi U-3210 spectrophotometer and a JEOL IR-810 spectrophotometer, respectively. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL JNM-GX-400 spectrometer at 399.78 MHz and at 100.43 MHz, respectively, or ^{1}H-NMR spectra were taken with a JEOL JNM-GX-270 spectrometer at 270.17 MHz, using tetramethylsilane as an internal standard. The coupling patterns are indicated as follows: singlet = s, doublet = d, triplet = t, quartet = q, multiplet = m, and broad = br. CD curves were determined on a JASCO J-600 spectropolarimeter. Column chromatography was performed using Kieselgel 60 (Art. 7734, Merck). LPLC was performed on a Chemco Low-prep 81-M-2 pump and a glass column (200 × 10 mm) packed with Silica gel CQ-3 (30—50 μm, Wako). Thin layer chromatography (TLC) was conducted on pre-coated Kieselgel 60 F_{254} (Art. 5715, Merck). Spots on TLC were detected by their absorption and/or fluorescence under UV light.

Isolation of Talaroderxines from *T. derxii* *T. derxii*, strain NHL 2981 (mating type A), was cultivated on rice (3.5 kg using 25 Roux flasks) at 25 °C for 21 d, and was extracted with CH_2Cl_2. After evaporation of the solvent *in vacuo*, the residue (25 g) was extracted with C_6H_6, washed with C_6H_{12} and evaporated. This residue (6.0 g) was crystallized from C_6H_6 to give talaroderxine (**1**) [a mixture of talaroderxines A (**1a**) and B (**1b**)] (1.95 g).

Acetylation of Talaroderxine (1) Talaroderxine (**1**) (50 mg) was acetylated with a mixture of Ac_2O (2 ml) and pyridine (2 ml) overnight at room temperature. The reaction mixture was poured into ice-water, acidified with 4 N HCl, and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated, and the residue was purified by repeated LPLC using the solvent system of C_6H_6–Me_2CO (20 : 1 and 17 : 1, v/v, respectively) to give pure talaroderxine A hexaacetate (**2a**) (18 mg) and talaroderxine B hexaacetate (**2b**) (21 mg).

Talaroderxine A Hexaacetate (**2a**): Amorphous powder with bluish violet fluorescence, $[\alpha]_D^{20}$ +98.1° (c = 0.77, MeOH). EI-MS *m/z* (%): 784 [(M − Ac)$^+$, 5], 742 [(M − Ac × 2)$^+$, 19], 700 [(M − Ac × 3)$^+$, 20], 658 [(M − Ac × 4)$^+$, 59], 616 [(M − Ac × 5)$^+$, 52], 574 [(M − Ac × 6)$^+$, 53]. FAB-MS *m/z* (%): 849 [(M + Na)$^+$, 10]. UV λ_{max}^{MeOH} nm (log ε): 243 (4.89), 251 sh (4.85), 288 (4.09), 297 (4.11), 308 (4.04), 349 (3.74). IR ν_{max}^{KBr} cm^{-1}: 1775, 1720 (–COO–). ^{1}H-NMR ($CDCl_3$) δ: 0.920 (6H, t, J = 7.0 Hz, 13-H_3), 1.462 (4H, m, 12-H_2), 1.606 (2H, m, 11-H), 1.767 (2H, 11-H), 1.900 (6H, s, 9-OAc), 2.474 (6H, s, 10-OAc), 2.539 (6H, s, 7-OAc), 2.857 (2H, m, 4-H), 2.943 (2H, m, 4-H), 4.428 (2H, m, 3-H), 6.970 (2H, br s, 8-H), 7.209 (2H, s, 5-H). CD ($c = 2.6 \times 10^{-6}$, MeOH) [θ] (nm): -5.70×10^5 (239), $+4.61 \times 10^5$ (263), -4.70×10^4 (311).

Talaroderxine B Hexaacetate (**2b**): Amorphous powder with bluish violet fluorescence, $[\alpha]_D^{20}$ +62.0° (c = 0.77, MeOH). EI-MS *m/z* (%): 784 [(M − Ac)$^+$, 7], 742 [(M − Ac × 2)$^+$, 22], 700 [(M − Ac × 3)$^+$, 40], 658 [(M − Ac × 4)$^+$, 69], 616 [(M − Ac × 5)$^+$, 81], 574 [(M − Ac × 6)$^+$, 56]. FAB-MS *m/z* (%): 849 [(M + Na)$^+$, 12]. UV λ_{max}^{MeOH} nm (log ε): 243 (4.89), 252 sh (4.84), 288 (4.04), 297 (4.08), 308 (4.04), 349 (3.74). IR ν_{max}^{KBr} cm^{-1}: 1775, 1720 (–COO–). ^{1}H-NMR ($CDCl_3$) δ: 0.913 (6H, t, J = 7.3 Hz, 13-H_3), 1.473 (4H, m, 12-H_2), 1.597 (2H, m, 11-H), 1.760 (2H, 11-H), 1.857 (6H, s, 9-OAc), 2.478 (6H, s, 10-OAc), 2.535 (6H, s, 7-OAc), 2.883 (4H, br s, 4-H_2), 4.410 (2H, m, 3-H), 6.954 (2H, br s, 8-H), 7.200 (1H, s, 5-H). CD ($c = 2.9 \times 10^{-6}$, MeOH) [θ] (nm): $+5.92 \times 10^5$ (240), -4.56×10^5 (264), $+4.52 \times 10^4$ (310).

Methanolysis of Talaroderxine A Hexaacetate (2a) Talaroderxine A hexaacetate (**2a**) (13 mg) was dissolved in MeOH (3 ml), and NaOMe (30 mg) was added. The mixture was stirred at room temperature for 25 min, acidified with 4 N HCl and extracted with $CHCl_3$, and then the extract was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by LPLC using the solvent system of $CHCl_3$–EtOH (20 : 1, v/v) to give talaroderxine A (**1a**) (9 mg).

Talaroderxine A (**1a**): Amorphous powder with yellow fluorescence, $[\alpha]_D^{20}$ −75.4° (c = 0.28, MeOH). EI-MS *m/z* (%): 574.1831 (M$^+$, 574.1837 for $C_{32}H_{30}O_{10}$, 100), 556 (16). UV λ_{max}^{MeOH} nm (log ε): 261 (4.84), 270 sh (4.79), 378 (4.27). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1640 (chelated –COO–). ^{1}H-NMR [$(CD_3)_2SO$] δ: 0.883 (6H, t, J = 7.0 Hz, 13-H_3), 1.405 (4H, m, 12-H_2), 1.548 (2H, m, 11-H), 1.675 (2H, m, 11-H), 2.748 (2H, dd, J = 15.8, 10.6 Hz, 4-H), 2.820 (2H, dd, J = 15.8, 4.6 Hz, 4-H), 4.552 (2H, m, 3-H), 6.219 (2H, s, 5-H), 6.599 (2H, s, 8-H), 9.681 (2H, s, 7-OH), 9.770 (2H, br, 9-OH), 13.350 (2H, br, 10-OH). CD ($c = 3.8 \times 10^{-5}$, MeOH) [θ] (nm): -2.67×10^5 (246), $+3.42 \times 10^5$ (267), -2.14×10^4 (320).

Methanolysis of Talaroderxine B Hexaacetate (2b) Talaroderxine B hexaacetate (**2b**) (13 mg) was methanolyzed in the same manner as described above. Purification by LPLC using the solvent system of $CHCl_3$–EtOH (20 : 1, v/v) gave talaroderxine B (**1b**) (8 mg).

Talaroderxine B (**1b**): Amorphous powder with yellow fluorescence, $[\alpha]_D^{20}$ −86.8° (c = 0.40, MeOH). EI-MS *m/z* (%): 574.1840 (M$^+$, 574.1837 for $C_{32}H_{30}O_{10}$, 100), 556 (15). UV λ_{max}^{MeOH} nm (log ε): 261 (4.82), 270 sh (4.76), 378 (4.24). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1640 (chelated –COO–). ^{1}H-NMR [$(CD_3)_2SO$] δ: 0.876 (6H, t, J = 7.0 Hz, 13-H_3), 1.399 (4H, m, 12-H_2), 1.601 (2H, m, 11-H), 1.661 (2H, m, 11-H), 2.695 (2H, dd, J = 15.8, 10.6 Hz, 4-H), 2.790 (2H, br d, J = 15.8 Hz, 4-H), 4.541 (2H, m, 3-H), 6.246 (2H, s, 5-H), 6.604 (2H, s, 8-H), 9.675 (2H, s, 7-OH), 9.770 (2H, br, 9-OH), 13.485 (2H, br, 10-OH). CD ($c = 3.5 \times 10^{-5}$, MeOH) [θ] (nm): $+2.33 \times 10^5$ (246), -3.06×10^5 (267), $+2.33 \times 10^4$ (320).

Methylation of Talaroderxine (1) with Dimethyl Sulfate Talaroderxine (**1**) (80 mg) was dissolved in Me_2CO (10 ml), and Me_2SO_4 (4 ml) and K_2CO_3 (100 mg) were added to the solution. After refluxing for 30 min, the mixture was poured into 5% NaOH to destroy the remaining Me_2SO_4,

and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and evaporated *in vacuo*, and the residue was purified by LPLC using the solvent system of C_6H_6–Me_2CO (10 : 1, v/v) to afford talaroderxine hexamethyl ether (**6**) (37 mg).

Talaroderxine Hexamethyl Ether (**6**): Pale yellow prisms with blue fluorescence, mp 231 °C (from C_6H_{14}–AcOEt), $[\alpha]_D^{24}$ +94.9° ($c=0.18$, $CHCl_3$). EI-MS *m/z*: 658.2781 (M^+, 100, Calcd for $C_{38}H_{42}O_{10}$: 658.2778). UV λ_{max}^{MeOH} nm (log ε): 219 (4.44), 257 (4.50), 269 (4.52), 351 (3.96). IR ν_{max}^{KBr} cm^{-1}: 1720 (–COO–). ^{1}H-NMR [$(CD_3)_2SO$] δ: 0.844 and 0.856 (6H, t, $J=7.1$ Hz, 13-H_3), 1.353 (4H, m, 12-H_2), 1.496 (2H, m, 11-H), 1.587 (2H, m, 11-H), 2.723 (4H, br s, 4-H_2), 3.711 and 3.783 (6H, s, 7-OMe), 3.896 and 3.903 (6H, s, 10-OMe), 4.103 and 4.106 (6H, s, 9-OMe), 4.278 (2H, m, 3-H), 6.525 and 6.582 (2H, br s, 5-H), 7.000 (2H, s, 8-H). ^{1}H-NMR ($CDCl_3$) δ: 0.897 (6H, t, $J=6.8$ Hz, 13-H_3), 1.502 (6H, m, 12-H_2 and 11-H), 1.737 (2H, m, 11-H), 2.672 (2H, m, 4-H), 2.745 (2H, m, 4-H), 3.782 and 3.822 (6H, s, 7-OMe), 4.058 and 4.076 (6H, s, 10-OMe), 4.123 (6H, s, 9-OMe), 4.290 (2H, m, 3-H), 6.520 and 6.576 (2H, s, 5-H), 6.796 (2H, s, 8-H). CD ($c=1.7\times10^{-5}$, MeOH) [θ] (nm): $+3.82\times10^4$ (222). -7.4×10^3 (243), $+3.65\times10^4$ (258), -8.7×10^3 (345).

Ozonolysis of Talaroderxine (1) Ozone was introduced into a solution of talaroderxine (**1**) (200 mg) in MeOH (30 ml) at −60 °C for 3.5 h, and then the mixture was refluxed for 1 h after addition of 5% NaOH (10 ml) and 30% H_2O_2 (20 ml). The reaction mixture was acidified and extracted with $CHCl_3$, and the extract was dried (Na_2SO_4) and evaporated. The residue (60 mg) was purified by LPLC using the solvent system of $CHCl_3$–EtOH (30 : 1, v/v) to give a colorless viscous oil (12 mg), $[\alpha]_D^{24}$ +22.3° ($c=0.60$ in $CHCl_3$), which was identical with authentic (*S*)-(+)-3-hydroxyhexanoic acid[11] by comparison of the TLC behavior and ^{1}H-NMR spectrum. ^{1}H-NMR ($CDCl_3$) δ: 0.933 (3H, t, $J=7.0$ Hz), 1.452 (4H, m), 2.411 (1H, dd, $J=16.5$, 8.6 Hz), 2.547 (1H, dd, $J=16.5$, 3.7 Hz), 4.053 (1H, m).

Determination of Antibacterial Activity The antibacterial activity was determined by means of the paper disc assay with *B. subtilis* as the test organism. The assay plates were prepared using Antibiotic medium 3 (Difco) (0.35 g) and agar (0.40 g) in distilled water (20 ml). Bacteria cultivated with the above medium for 2 d were suspended in water and spread over the surface of the assay plates with cotton. The metabolites or their derivatives dissolved in Me_2CO or MeOH were charged onto paper discs (8 mm diameter) in the amounts mentioned in Table III, and the discs were dried and placed on the assay plates. Zones of inhibition (mm in diameter) were recorded after a 24 h incubation at 37 °C.

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References and Notes

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