Falconensins A, B, C, and D, New Compounds Related to Azaphilone, from *Emericella falconensis*

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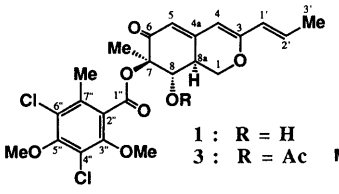
Four new compounds related to azaphilones, designated falconensins A (1), B (2), C (3), and D (4), were isolated from the mycelium of *Emericella falconensis*, a new ascomycetous fungus isolated from Venezuelan soil. The structures of falconensins A to D (1—4) were confirmed by spectroscopic investigation and chemical correlations. These falconensins are the hydrogenated azaphilones.

Keywords *Emericella falconensis*; azaphilone; falconensin A; falconensin B; falconensin C; falconensin D

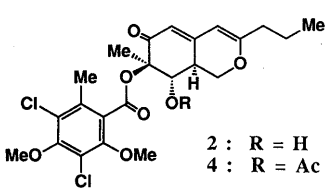
A new ascomycetous fungus, *Emericella falconensis* HORIE, MIYAJI, NISHIMURA *et* UDAGAWA (anamorph; *Aspergillus falconensis* HORIE, MIYAJI, NISHIMURA *et* UDAGAWA) was isolated from Venezuelan soil in 1988.[1] The mycelial dichloromethane extract of *E. falconensis*, strain NHL 2999 (=ATCC 76117), cultivated in Czapek medium supplemented with 0.2% yeast extract, had antibacterial activity against *Bacillus subtilis* COHN and antifungal activity against *Trichophyton mentagrophytes* (ROBIN) BLANCHARD. In the course of searching for antibacterial and/or antifungal metabolites, four new compounds designated falconensins A (**1**), B (**2**), C (**3**), and D (**4**) were isolated from the above extract. We now report the structural determination of **1**, **2**, **3**, and **4**.

Falconensins A (**1**), B (**2**), C (**3**), and D (**4**) showed positive coloration (green) in the Beilstein test, and gave molecular ion peaks at *m/z* 482, 484, and 486 (26 : 19 : 4), at *m/z* 484, 486, and 488 (15 : 10 : 2), at *m/z* 524, 526, and 528 (12 : 9 : 3), and at *m/z* 526, 528, and 530 (51 : 35 : 7), respectively, in the electron impact ionization (EI) mass spectra. The above results indicated that **1**, **2**, **3**, and **4** possess two chlorine atoms in each molecule. Elemental analysis and/or high resolution mass spectrometry confirmed the molecular formulae of **1**, **2**, **3**, and **4** as $C_{23}H_{24}Cl_2O_7$, $C_{23}H_{26}Cl_2O_7$, $C_{25}H_{26}Cl_2O_8$, and $C_{25}H_{28}Cl_2O_8$, respectively.

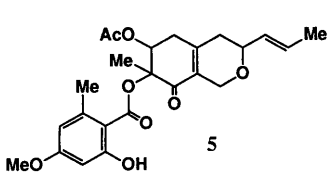
The infrared (IR) absorption of falconensin A (**1**) at 1735 cm^{-1} suggested the presence of an ester. On methanolysis with sodium methoxide using the same procedure as in the case of wortmin (**5**), an azaphilone-related compound, isolated from *Penicillium wortmannii* KLOCKER [=*Talaromyces wortmannii* (KLOCKER) C. R. BENJAMIN],[2] **1** gave only methyl dichlorodimethoxymethylbenzoate (**6**) as an isolable product. Compound **6** was hydrolyzed by alkali to give the corresponding acid (**7**). The structures of **7** was confirmed as 3,5-dichloro-2,4-dimethoxy-6-methylbenzoic acid by comparison of the IR and proton nuclear magnetic resonance (^{1}H-NMR) spectra and by mixed fusion with an authentic sample, which was synthesized from ethyl dihydroorsellinate in four steps according to the literature.[3,4] These results confirmed the benzoate part structure of falconensin A (**1**).



1 : R = H
3 : R = Ac



2 : R = H
4 : R = Ac



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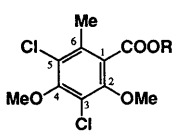


6 : R = Me
7 : R = H

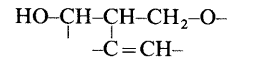
The benzoate part ($C_{10}H_9Cl_2O_3$) of falconensin A (**1**) showed fragment ion peaks at *m/z* 247, 249, and 251 (98 : 64 : 11) in the EI mass spectrum, whereas the base peak was observed at *m/z* 235 ($C_{13}H_{15}O_4$) due to the remaining alcohol part. Decoupling experiments as well as the ^{1}H-NMR, the carbon-13 nuclear magnetic resonance (^{13}C-NMR), and the ^{1}H–^{13}C shift correlated (COSY) spectra of **1** (Table) were used to deduce the partial structure

TABLE I. ^{1}H- and ^{13}C-NMR Chemical Shift Correlations of Falconensin A (**1**) in $CDCl_3$

No.	δ_C (ppm)	δ_H (ppm)	J (Hz)	Correlated carbon signals with the proton on the same line in the COLOC spectrum
1	68.50 (Tdd)[a]	3.84 (dd)	13.1, 10.7	
		4.80 (dd)	10.7, 5.2	
3	160.65 (m)			
4	102.68 (Dbrd)	5.57 (s)		C-3, C-5, C-1′
4a	150.41 (brs)			
5	116.50 (Ddd)	5.81 (d)	1.8	C-4, C-7
6	193.29 (d)			
7	86.53 (m)			
7-Me	16.86 (Qd)	1.49 (s)		C-6, C-7, C-8
8	70.06 (Dm)	4.72 (dd)	10.4, 3.1	
8-OH	—	2.79 (d)	3.1	
8a	38.05 (Ddd)	2.88 (dddd)	13.1, 10.4, 5.2, 1.8	
1′	125.41 (Ddd)	5.91 (dq)	15.6, 1.5	C-3
2′	134.03 (Dq)	6.47 (dq)	15.6, 7.0	
3′	18.38 (Qdd)	1.87 (dd)	7.0, 1.5	C-1′, C-2′
1″	164.46 (s)			
2″	126.44 (q)[b]			
3″	151.88 (q)[c]			
3″-OMe	62.52 (Q)[d]	3.90 (s)[b]		C-3″
4″	120.66 (s)			
5″	154.32 (q)[c]			
5″-OMe	60.64 (Q)[d]	3.91 (s)[b]		C-5″
6″	126.61 (q)[b]			
7″	134.51 (q)			
7″-Me	17.21 (Q)	2.48 (s)		C-2″, C-6″, C-7″

a) The multiplicity is indicated. *b, c, d*) The assignments may be reversed.

of the alcohol part in **1**. When the vinylic proton at δ6.47 (dq) was irradiated, the methyl protons at δ 1.87 (dd) and the vinylic proton at δ 5.91 (dq) were changed into a doublet and a broad singlet, respectively. Moreover, irradiation of the proton at δ 5.91 caused a change of the signals at δ 6.47 (q) and 1.87 (d). The above results suggested the presence of a 1-propenyl residue in the molecule of **1**. The double doublets at δ 4.80 and 3.84, which corresponded to the protons attached to carbon (δ 68.50) bearing an oxygen, and at δ4.72, which corresponded to the proton attached to carbon (δ70.06) bearing a hydroxy group, were all changed to doublets when the signal at δ 2.88 (dddd) was irradiated. This irradiation also caused a change of the vinylic proton at δ 5.81 from doublet to singlet. Therefore the presence of the partial structure



was confirmed in **1**. The remaining protons of the alcohol part of **1** were a vinylic proton at δ5.57 and methyl protons at δ 1.49.

The correlation peaks in the ^1H–^{13}C long-range shift correlated (COLOC) spectrum of **1** are listed in Table. The tertiary methyl protons at δ 1.49 were correlated with the conjugated carbonyl carbon at δ 193.29 (C-6), oxygen-bearing carbon at δ 86.53 (C-7), and the carbon bearing the hydroxy group at δ 70.06 (C-8). Correlation peaks of the vinylic proton at δ 5.81, which coupled allylically with the proton at δ 2.88 were observed with the carbons at δ 86.53 (C-7) and 102.68 (C-4). The other vinylic proton at δ 5.57 was correlated with the carbons at δ 116.50 (C-5), 160.65 (C-3), and 125.41 (C-1′). Furthermore, nuclear Overhauser enhancements (NOE) were observed on the vinylic protons at δ 5.91 and 5.81 when the vinylic proton at δ 5.57 was irradiated. From the above results, the structure of falconensin A (**1**) was concluded to be 7-(3,5-dichloro-2,4-dimethoxy-6-methylbenzoyl)-8-hydroxy-7-methyl-3-(1-propenyl)-1,7,8,8a-tetrahydro-6*H*-2-benzopyran-6-one.

Difference NOE experiments in conjunction with measurements of scalar coupling constants in the ^1H-NMR spectrum of **1** (Table) were conducted to determine the relative stereochemistry. When the proton signal of 8a-H (δ 2.88) was irradiated, NOE was observed at the tertiary methyl group at C-7 (δ 1.49) and one of the methylene protons at C-1 (δ 4.80). On the other hand, irradiation of the above methyl protons caused enhancement of the same proton at C-8a. These observations confirmed that the stereochemical relationship between the methyl at C-7 and the proton at C-8a is *cis* on the cyclohexenone ring. The large coupling constant (10.4 Hz) of 8-H (δ 4.72) and 8a-H indicated that these two protons have *trans*-diaxial configuration. Thus, the relative stereochemistry of falconensin A (**1**) was determined.

The ^1H-NMR spectra of falconensins B (**2**), C (**3**), and D (**4**) resemble those of falconensin A (**1**). The ultraviolet (UV) spectra of **1** and **3** showed maxima at 349 and 344 nm, respectively, whereas **2** and **4** both had a UV maximum at 323 nm. The above results suggested that **2** and **4** had one less conjugated double bond than **1** and **3**. Instead of the ^1H-NMR signals assigned to the 2-propenyl residue at C-3 [δ 1.87 (3H), 5.91 (1H), and 6.47 (1H) in **1**: δ 1.87 (3H), 5.90 (1H), and 6.45 (1H) in **3**], signals at δ 0.95 (3H), 1.60 (2H), 2.18 (1H), and 2.25 (1H) in **2** and those at δ 0.94 (3H), 1.60 (2H), 2.18 (1H), and 2.21 (1H) in **4** appeared. Hydrogenation of **1** and **3** on 5% Pd–C gave **2** and **4**, respectively, as the main products, which were identical with the natural products, including the circular dichroism (CD) curves. These results indicated that the side chain at C-3 in **2** and **4** is not a 2-propenyl residue, but a propyl residue. On acetylation, **1** and **2** gave quantitatively **3** and **4**, respectively, indicating the presence of one acetoxyl group in **3** (δ 2.18) and **4** (δ 2.17). Since the proton attached at C-8 in **1** and **2** (δ 4.72 and 4.71, respectively) was shifted more than 1 ppm downfield in **3** and **4** (δ 6.09 and 6.07, respectively), it is clear that the acetylation occurred at the hydroxy group at C-8 in **1** and **2**. The relative structures of falconensins B, C, and D were thus confirmed as **2**, **3**, and **4**, respectively.

Falconensins A (**1**), B (**2**), C (**3**), and D (**4**) are hydrogenated azaphilones with a dichloroorsellinate moiety. These compounds (**1**—**4**) showed no antibacterial or antifungal activity against *B. subtilis* and *T. mentagrophytes*.

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. EI-MS were taken with a JEOL JMD-D-300 spectrometer. UV and IR spectra were recorded on a Hitachi U-3210 spectrophotometer and a JASCO IR-810 spectrophotometer, respectively. ^1H-NMR 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 ^1H-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 or d, triplet = T or t, quartet = Q or q, multiplet = m, and broad = br. Capital letters refer to the pattern resulting from directly bonded coupling ($^1J_{C,H}$). CD curves were determined on a JASCO J-600 spectropolarimeter. Column chromatography was performed using Kieselgel 60 (Art. 7734; Merck). Low pressure liquid chromatography (LPLC) was performed with a Chemco Low-Prep 81-M-2 pump and a glass column (10 i.d. × 150 or 200 mm) packed with Silica gel CQ-3 (30—50 μm, Wako). TLC was conducted on pre-coated Kieselgel 60 F_{254} plates (Art. 5715, Merck). Spots on TLC plates were detected on the basis of their absorption of UV light.

Isolation of Falconensins from *E. falconensis* *E. falconensis*, strain NHL 2999, was cultivated in Czapek medium supplemented with 0.2% yeast extract (30 l) using 120 Roux flasks at 25 °C for 21 d. The dried mycelium (227 g) was extracted with CH_2Cl_2 and the organic layer was dried with Na_2SO_4 and then evaporated *in vacuo*. The extract obtained (17.9 g) was chromatographed on silica gel with benzene–AcOEt (20 : 1) to give the falconensins-containing fraction (3.0 g), and with benzene–AcOEt (2 : 1) to afford ergosterol. The former fraction was purified by repeated LPLC with hexane–acetone (40 : 1) to afford falconensin D (**4**) (12 mg) and falconensin C (**3**) (7 mg), with hexane–acetone (20 : 1) to afford falconensin B (**2**) (287 mg), and with hexane–acetone (10 : 1) to give falconensin A (**1**) (361 mg).

Falconensin A (**1**): Pale yellow needles with blue fluorescence, mp 84 °C (from hexane–CH_2Cl_2). Beilstein test: positive (green). $[\alpha]_D^{20}$ +238° (c = 0.25, MeOH). *Anal.* Calcd for $C_{23}H_{24}Cl_2O_7$: C, 57.15; H, 5.00. Found: C, 57.00; H, 5.03. EI-MS m/z (%): 482.0894 (M^+, 482.0897 for $C_{23}H_{24}{}^{35}Cl_2O_7$, 26), 484.0873 (M + 2, 484.0870 for $C_{23}H_{24}{}^{35}Cl^{37}ClO_7$, 19), 486.0845 (M + 4, 486.0840 for $C_{23}H_{24}{}^{37}Cl_2O_7$, 4), 246.9930 (246.9929 for $C_{10}H_9Cl_2O_3$, 98), 249 (64), 251 (11), 235.0966 (235.0968 for $C_{13}H_{15}O_4$, 100). UV λ_{max}^{MeOH} nm (log ε): 273 sh (3.76), 349 (4.57). IR ν_{max}^{KBr} cm^{-1}: 3600—3200 (OH), 1735 (–COO–), 1665 (conjugated C=O). ^1H-NMR ($CDCl_3$) δ: 1.49 (3H, s, 7-Me), 1.87 [3H, dd, J = 7.0, 1.5 Hz, 3′-H_3 (Me)], 2.48 (3H, s, 7″-Me), 2.79 (1H, d, J = 3.1 Hz, 8-OH), 2.88 (1H, dddd, J = 13.1, 10.4, 5.2, 1.8 Hz, 8a-H), 3.84 [1H, dd, J = 13.1, 10.7 Hz, 1-H (ax.)], 3.90 (3H, s, 3″- or 5″-OMe), 3.91 (3H, s, 5″- or 3″-OMe), 4.72 (1H, dd, J = 10.4, 3.1 Hz, 8-H), 4.80 [1H, dd, J = 10.7, 5.2 Hz, 1-H (eq.)], 5.57 (1H, s, 4-H),

5.81 (1H, d, J=1.8 Hz, 5-H), 5.91 (1H, dq, J=15.6, 1.5 Hz, 1′-H), 6.47 (1H, dq, J=15.6, 7.0 Hz, 2′-H). CD (c=2.1×10^{-5}, MeOH) $\Delta\varepsilon^{20}$ (nm): −1.1 (206), +5.4 (225), −0.5 (244), +0.8 (276), −3.0 (320), +12.4 (366), +7.0 (385).

Falconensin B (**2**): Colorless prisms with blueish violet fluorescence, mp 130 °C (from MeOH). Beilstein test: positive (green), $[\alpha]_D^{20}$ +151° (c=0.25, MeOH). EI-MS m/z (%): 484.1059 (M^+, 484.1056 for $C_{23}H_{26}{}^{35}Cl_2O_7$, 15), 486.1017 (M+2, 484.1024 for $C_{23}H_{26}{}^{35}Cl^{37}ClO_7$, 10), 488.0995 (M+4, 488.0995 for $C_{23}H_{26}{}^{37}Cl_2O_7$, 2), 247 ($C_{10}H_9Cl_2O_3$, 100), 249 (64), 251 (12), 237 ($C_{13}H_{17}O_4$, 51). UV λ_{max}^{MeOH} nm (log ε): 323 (4.31). IR ν_{max}^{KBr} cm^{-1}: 3600—3400 (OH), 1735 (–COO–), 1670 (conjugated C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.95 [3H, t, J=7.3 Hz, 3′-H$_3$ (Me)], 1.49 (3H, s, 7-Me), 1.60 (2H, qt, J=7.3, 7.3 Hz, 2′-H), 2.18 (1H, dt, J=13.7, 7.3 Hz, 1′-H), 2.25 (1H, dt, J=13.7, 7.3 Hz, 1′-H), 2.49 (3H, s, 7″-Me), 2.82 (1H, d, J=3.1 Hz, 8-OH), 2.86 (1H, dddd, J=13.1, 10.4, 4.9, 1.8 Hz, 8a-H), 3.82 [1H, dd, J=13.1, 10.7 Hz, 1-H (ax.)], 3.90 (3H, s, 5″- or 3″-OMe), 3.91 (3H, s, 3″- or 5″-OMe), 4.71 (1H, dd, J=10.4, 3.1 Hz, 8-H), 4.77 [1H, dd, J=10.7, 4.9 Hz, 1-H (eq.)], 5.52 (1H, s, 4-H), 5.74 (1H, d, J=1.8 Hz, 5-H). ^{13}C-NMR ($CDCl_3$) δ: 13.57 (Qdt, C-3′), 16.85 (Qd, 7-Me), 17.16 (Q, 7″-Me), 20.02 (Tq, C-2′), 36.53 (Tm, C-1′), 37.73 (Dm, C-8a), 60.62 (Q, 3″- or 5″-Me), 62.47 (Q, 5″- or 3″-Me), 68.70 (Tdd, C-1), 70.12 (Dm, C-8), 86.47 (m, C-7), 100.82 (Ddt, C-4), 115.37 (Ddd, C-5), 120.66 (s, C-4″), 126.39 (q, C-2″ or -6″), 126.64 (q, C-6″ or -2″), 134.47 (q, C-7″), 150.38 (br s, C-4a), 151.91 (q, C-3″ or -C-5″), 154.29 (q, C-5″ or C-3″), 164.46 (s, C-1″), 168.45 (m, C-3), 193.56 (br s, C-6). CD (c=2.7×10^{-5}, MeOH) $\Delta\varepsilon^{20}$ (nm): −2.8 (212), +1.1 (227), −3.0 (307), +7.8 (342), +7.0 (352).

Falconensin C (**3**): Pale yellow crystalline powder with blue fluorescence, mp 152 °C (from hexane–CH_2Cl_2). Beilstein test: positive (green), $[\alpha]_D^{20}$ +301° (c=0.05, MeOH). EI-MS m/z (%): 524.0997 (M^+, 524.1003 for $C_{25}H_{26}{}^{35}Cl_2O_8$, 12), 526.0983 (M+2, 526.0976 for $C_{25}H_{26}{}^{35}Cl^{37}ClO_8$, 9), 528.0938 (M+4, 528.0944 for $C_{25}H_{26}{}^{37}Cl_2O_8$, 3), 247 ($C_{10}H_9Cl_2O_3$, 47), 249 (29), 251 (6), 235 ($C_{13}H_{15}O_4$, 100). UV λ_{max}^{MeOH} nm (log ε): 344 (4.39). IR ν_{max}^{KBr} cm^{-1}: 1740 (–COO–), 1660 (conjugated C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.57 (3H, s, 7-Me), 1.87 [3H, dd, J=7.5, 1.5 Hz, 3′-H$_3$ (Me)], 2.18 (3H, s, 8-OAc), 2.50 (3H, s, 7″-Me), 2.99 (1H, dddd, J=13.4, 11.0, 4.9, 2.4 Hz, 8a-H), 3.83 (3H, s, 3″- or 5″-OMe), 3.88 (3H, s, 5″- or 3″-OMe), 3.97 [1H, dd, J=13.4, 11.0 Hz, 1-H (ax.)], 4.34 [1H, dd, J=11.0, 4.9 Hz, 1-H (eq.)], 5.59 (1H, s, 4-H), 5.86 (1H, d, J=2.4 Hz, 5-H), 5.90 (1H, dq, J=15.4, 1.5 Hz, 1′-H), 6.09 (1H, d, J=11.0 Hz, 8-H), 6.45 (1H, dq, J=15.4, 7.5 Hz, 2′-H). CD (c=2.3×10^{-5}, MeOH) $\Delta\varepsilon^{20}$ (nm): +2.2 (217), −2.1 (241), +10.4 (359), +9.7 (371).

Falconensin D (**4**): Pale yellow crystalline powder with blueish violet fluorescence, mp 71 °C. Beilstein test: positive (green), $[\alpha]_D^{20}$ +196° (c=0.22, MeOH). EI-MS m/z (%): 526.1153 (M^+, 526.1159 for $C_{25}H_{28}{}^{35}Cl_2O_8$, 51), 528.1128 (M+2, 528.1130 for $C_{25}H_{28}{}^{35}Cl^{37}ClO_8$, 35), 530.1096 (M+4, 530.1101 for $C_{25}H_{28}{}^{37}Cl_2O_8$, 7), 247 ($C_{10}H_9Cl_2O_3$, 51), 249 (31), 251 (6), 235 ($C_{13}H_{17}O_4$, 100). UV λ_{max}^{MeOH} nm (log ε): 323 (4.23). IR ν_{max}^{NaCl} cm^{-1}: 1750 (–COO–), 1670 (conjugated C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.94 [3H, t, J=7.3 Hz, 3′-H$_3$ (Me)], 1.56 (3H, s, 7-Me), 1.60 (2H, tq, J=7.5, 7.3 Hz, 2′-H), 2.17 (3H, s, 8-OAc), 2.21 (1H, dt, J=13.7, 7.5 Hz, 1′-H), 2.25 (1H, td, J=7.5, 3.1 Hz, 1′-H), 2.50 (3H, s, 7″-Me), 2.93 (1H, dddd, J=13.4, 10.4, 5.5, 1.8 Hz, 8a-H), 3.81 (3H, s, 5″- or 3″-OMe), 3.88 (3H, s, 3″- or 5″-OMe), 3.91 [1H, dd, J=13.4, 11.0 Hz, 1-H (ax.)], 4.30 [1H, dd, J=11.0, 5.5 Hz, 1-H (eq.)], 5.54 (1H, s, 4-H), 5.78 (1H, d, J=1.8 Hz, 5-H), 6.07 (1H, d, J=10.4 Hz, 8-H). CD (c=3.9×10^{-5}, MeOH) $\Delta\varepsilon^{20}$ (nm): −2.5 (233), −2.0 (241), −1.0 (302), +3.9 (328), +8.1 (342), +7.0 (355).

Methanolysis of Falconensin A (1) Falconensin A (**1**) (45 mg) was dissolved in MeOH (2 ml), and NaOMe (11.8 mg) was added. The mixture was refluxed for 20 min, then the solvent was evaporated *in vacuo*. The residue was acidified with dilute HCl and extracted with $CHCl_3$. The extract was dried over Na_2SO_4 and the solvent was removed by evaporation. The residue was purified by LPLC (benzene) to give methyl 3,5-dichloro-2,4-dimethoxy-6-methylbenzoate (**6**) (22 mg, 85%).

Compound **6**: White amorphous powder. Beilstein test: positive (green). EI-MS m/z (%): 278 (M^+, 45), 280 (M+2, 30), 282 (M+4, 6). UV λ_{max}^{MeOH} nm (log ε): 280 (3.28). IR ν_{max}^{KBr} cm^{-1}: 1715 (–COO–). ^{1}H-NMR ($CDCl_3$) δ: 2.30 (3H, s, 6-Me), 3.88 (3H, s, OMe), 3.90 (3H, s, OMe), 3.94 (3H, s OMe). ^{13}C-NMR ($CDCl_3$) δ: 17.40 (6-Me), 52.64 (COO<u>Me</u>), 60.61 (OMe), 62.16 (OMe), 121.20 (C-3), 127.00 (C-1 or -5), 128.32 (C-5 or -1), 133.37 (C-6), 152.39 (C-2 or -4), 154.14 (C-4 or -2), 166.90 (<u>C</u>OOMe).

Hydrolysis of Methyl 3,5-Dichloro-2,4-dimethoxy-6-methylbenzoate (6) A 10% NaOH solution (2 ml) was added to a solution of **6** (30 mg) in MeOH (1 ml), and the mixture was left at 60 °C for 12 h. After cooling, the reaction mixture was acidified with 4 N HCl and extracted with $CHCl_3$, then the solvent was evaporated off *in vacuo*. The residue was crystallized from hexane–CH_2Cl_2 to give 3,5-dichloro-2,4-dimethoxy-6-methylbenzoic acid (**7**) (21 mg, 74%). This compound (**7**) was identical with an authentic specimen synthesized from ethyl dihydroorsellinate[3,4] on the basis of IR and ^{1}H-NMR spectral comparison and mixed fusion.

3,5-Dichloro-2,4-dimethoxy-6-methylbenzoic Acid (**7**): Colorless needles, mp 135 °C (from hexane–CH_2Cl_2). Beilstein test: positive (green). EI-MS m/z (%): 264 (M^+, 43), 266 (M+2, 27), 268 (M+4, 5). IR ν_{max}^{KBr} cm^{-1}: 3200—2400 (COOH), 1690 (COOH). ^{1}H-NMR ($CDCl_3$) δ: 2.43 (3H, s, 6-Me), 3.92 (3H, s, OMe), 3.95 (3H, s, OMe).

Hydrogenation of Falconensins A (1) and C (3) with 5% Pd/C A suspension of 5% Pd/C (5 mg) in a solution of falconensin A (**1**) (60 mg) or C (**3**) (55 mg) in MeOH (5 ml) was stirred at room temperature in a hydrogen atmosphere for 7 min. After filtration to remove the catalyst, the solvent was evaporated off *in vacuo*. The residue was purified by LPLC using the solvent system of hexane–acetone (20 : 1) to afford dihydrofalconensin A (**2**) or D (**4**) (22 mg), which was identical with falconensins B and D, respectively, on the basis of ^{1}H-NMR, UV, IR, and CD spectral comparison, TLC behavior, and mixed melting point determination.

Acetylation of Falconensins A (1) and B (2) Falconensin A (**1**) (47 mg) or B (**2**) (57 mg) was dissolved in a mixture of pyridine (0.5 ml) and Ac_2O (0.25 ml), and the solution was kept overnight at room temperature, then poured into ice-water and extracted with ether. The extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by LPLC using the solvent system of hexane–acetone (40 : 1) to afford mono-*O*-acetylfalconensin A (**3**) (37 mg) or B (**4**) (38 mg), which was identical with the naturally occurring falconensin C or D, respectively, on the basis of ^{1}H-NMR, UV, IR, and CD spectral comparison, TLC behavior, and mixed melting point determination.

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