Tetrahedron 66 (2010) 2594–2597

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Phomactin I, 13-*epi*-Phomactin I, and Phomactin J, three novel diterpenes from a marine-derived fungus

Masahiro Ishino [a], Nobuto Kiyomichi [a], Kazuhiko Takatori [b], Takashi Sugita [c], Motoo Shiro [d], Kaoru Kinoshita [a], Kunio Takahashi [a], Kiyotaka Koyama [a,*]

[a] *Department of Pharmacognosy and Phytochemistry, Meiji Pharmaceutical University, Noshio 2-522-1, Kiyose-shi, Tokyo 204-8588, Japan*
[b] *Department of Synthetic Organic Chemistry, Meiji Pharmaceutical University, Noshio 2-522-1, Kiyose-shi, Tokyo 204-8588, Japan*
[c] *Department of Microbiology, Meiji Pharmaceutical University, Noshio 2-522-1, Kiyose-shi, Tokyo 204-8588, Japan*
[d] *X-ray Research Laboratory, Rigaku Corporation, Matsubara-cho 3-9-12, Akishima-shi, Tokyo 196-8666, Japan*

ARTICLE INFO

Article history:
Received 19 November 2009
Received in revised form 6 February 2010
Accepted 8 February 2010
Available online 13 February 2010

ABSTRACT

Three novel diterpenes were isolated from cultures of an unidentified marine-derived fungus. The structures of the compounds, phomactin I (**1**), 13-*epi*-phomactin I (**2**), and phomactin J (**3**) were determined by spectroscopic and X-ray crystallographic methods.

© 2010 Elsevier Ltd. All rights reserved.

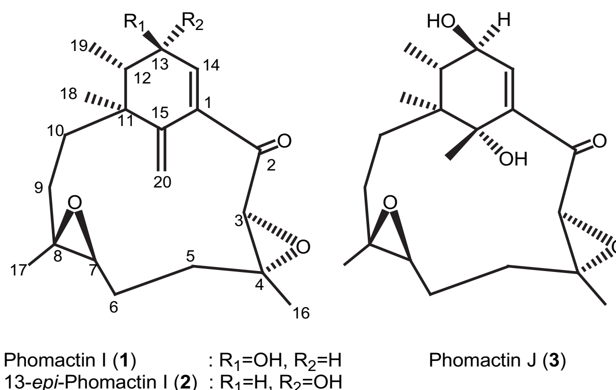
1. Introduction

Marine-derived fungi have the potential to produce unique secondary metabolites with diverse biological activities. In addition, these fungi are relatively easy to cultivate. Therefore, marine-derived fungi represent a useful resource in the search for new pharmaceutical compounds. We reported previously the isolation of phomactin H from an unidentified fungus (MPUC 046).[1] Here, we describe the isolation and structure elucidation of novel phomactin I (**1**), 13-*epi*-phomactin I (**2**), and phomactin J (**3**).

An unidentified fungus (MPUC 046) was isolated from the surface of the marine brown alga *Ishige okamurae*, collected at Tateishi, Kanagawa Prefecture, Japan, in September 2000. The D1/D2 26S rDNA and internal transcribed spacer regions, including 5.8S rDNA in the rRNA gene of the isolate, were directly sequenced using PCR. The sequence data (approximately 1200 bp long) were searched using the BLAST system (http://www.ncbi.nlm.nih.gov/BLAST/) at GenBank. The isolate was not assigned to any known species, but it belongs to Dothideales, phylogenetically. MPUC046 was not closely related to *Phoma* sp. producing phomactins[2–7] on a molecular phylogenetic tree.

2. Results and discussion

Phomactin I (**1**) was obtained as a white powder that was recrystallized as colorless prisms. The molecular formula for **1** was determined to be $C_{20}H_{28}O_4$ (seven degrees of unsaturation) by HR-EIMS analysis (332.1987: M^+ calcd for 332.1988). The IR spectrum of **1** indicated the presence of hydroxyl (3510 cm^{-1}) and carbonyl (1700 cm^{-1}) groups.



The ^{13}C NMR and DEPT data of **1** (Table 1) indicated the presence of a ketone (δ_C 199.5, C-2), four olefinic carbons (δ_C 143.9, C-15; 141.8, C-1; 129.5, C-14; 118.5, C-20), three singlet methyl carbons (δ_C 21.5, C-18; 19.1, C-17; 13.8, C-16), a doublet methyl carbon (δ_C 15.5, C-19), four methylene carbons (δ_C 35.7, C-5; 30.3, C-9; 28.3, C-10; 24.4, C-6), three oxymethine carbons (δ_C 71.5 C-13; 64.4 C-3; 55.7, C-7), a methine carbon (δ_C 46.1, C-12), two quaternary oxycarbons (δ_C 63.2, C-4; 58.9, C-8) and a quaternary carbon (δ_C 41.5, C-11). ^1H NMR, HMQC, and DQF-COSY data of **1** (Tables 1 and 2) showed the presence of four fragments, C-5–C-6–C-7, C-9–C-10, C-12–C-19, and C-13–C-14. Further information regarding the skeletal framework was obtained from HMBC (Table 3).

* Corresponding author.
E-mail address: Kiyotaka@my-pharm.ac.jp (K. Koyama).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.02.040

Table 1
^{13}C and ^{1}H NMR spectra of **1**, **2** in $CDCl_3$ and **3** in DMSO-d_6 (δ ppm)

Position	1		2		3	
	$\delta^{13}C$	$\delta^{1}H$	$\delta^{13}C$	$\delta^{1}H$	$\delta^{13}C$	$\delta^{1}H$
1	141.8 s		142.7 s		149.5 s	
2	199.5 s		198.2 s		199.8 s	
3	64.4 d	3.83 (1H, s)	64.7 d	3.84 (1H, s)	66.3 d	4.02 (1H, s)
4	63.2 s		62.9 s		62.8 s	
5	35.7 t	1.10 (1H, m) 2.26 (1H, ddd, 13.3, 4.3, 3.2)	35.5 t	1.09 (1H, m) 2.26 (1H, ddd, 13.4, 4.6, 3.1)	34.0 t	1.41 (1H, m) 2.07 (1H, m)
6	24.4 t	1.47 (1H, m) 2.16 (1H, m)	24.2 t	1.48 (1H, m) 2.13 (1H, m)	24.2 t	1.23 (1H, m) 2.07 (1H, m)
7	55.7 d	2.89 (1H, dd, 10.7, 4.0)	55.5 d	2.80 (1H, dd, 10.9, 3.8)	60.4 d	2.51 (1H, m)
8	58.9 s		59.1 s		62.2 s	
9	30.3 t	1.53 (1H, ddd, 15.7, 7.3, 1.4) 2.05 (1H, ddd, 15.7, 10.5, 7.3)	28.8 t	1.62 (1H, ddd, 15.8, 5.9, 2.5) 2.01 (1H, m)	33.8 t	0.98 (1H, m) 1.73 (1H, m)
10	28.3 t	1.16 (1H, m) 1.70 (1H, m)	26.3 t	1.20 (2H, m)	39.0 t	1.45 (1H, m) 1.55 (1H, m)
11	41.5 s		45.8 s		41.2 s	
12	46.1 d	1.73 (1H, m)	44.3 d	1.92 (1H, m)	42.0 d	1.41 (1H, m)
13	71.5 d	4.06 (1H, d, 4.3)	67.6 d	4.74 (1H, m)	71.4 d	4.00 (1H, m)
14	129.5 d	5.92 (1H, d, 4.3)	132.0 d	5.83 (1H, m)	136.6 d	5.61 (1H, d, 1.8)
15	143.9 s		143.7 s		75.4 s	
16	13.8 q	1.32 (3H, s)	13.6 q	1.28 (3H, s)	14.2[a] q	1.22 (3H, s)
17	19.1 q	1.26 (3H, s)	18.9 q	1.26 (3H, s)	15.7[a] q	1.22 (3H, s)
18	21.5 q	1.06 (3H, s)	22.1 q	1.07 (3H, s)	19.3 q	0.98 (3H, s)
19	15.5 q	0.81 (3H, d, 7.3)	8.4 q	0.79 (3H, d, 6.9)	19.1 q	1.10 (3H, d, 7.3)
20	118.5 t	5.28 (2H, m)	117.5 t	5.19 (1H, br s) 5.26 (1H, br s)	21.3 q	1.38 (3H, s)
OH-13						5.00 (1H, d, 5.8)
OH-15						4.76 (1H, s)

[a] may be interchanged.

Table 2
DQF-COSY correlations of **1** and **2** in $CDCl_3$, and **3** in DMSO-d_6

Position	1	2	3
H-5	H-6	H-6	H-6
H-6	H-5, 7	H-5, 7	H-5, 7
H-7	H-6	H-6	H-6
H-9	H-10	H-10	H-10
H-10	H-9	H-9	H-9
H-12	H-19	H-13, 19	H-13, 19
H-13	H-14	H-12	H-12, OH-13
H-14	H-13	n.o.[a]	n.o.
H-19	H-12	H-12	H-12
OH-13			H-13

[a] n.o.=not obserbed.

Table 3
HMBC correlations of **1** and **2** in $CDCl_3$, and **3** in DMSO-d_6

Position	1	2	3
H-3	C-2, 4, 5	C-2, 4	C-1, 2, 4, 5
H-5	C-3, 4, 6, 7, 16	C-3, 6	C-3, 4
H-6	C-4	C-5	C-4, 8
H-7	C-6	n.o.[a]	n.o.
H-9	C-7, 8, 10, 11	C-7, 8, 10, 11	C-7, 8, 10
H-10	C-8, 9, 11, 15, 18	C-8, 15, 18	C-8, 9, 15
H-12	C-10, 11, 13, 14, 15, 19	C-11, 13, 15	C-18, 19
H-13	C-1, 11, 14, 19	C-1, 19	C-12, 14, 19
H-14	C-2, 12, 15	C-2, 12, 15	C-2, 12, 15
H-16	C-4, 5	C-4, 5	C-3, 4, 5, 8, 9[b]
H-17	C-7, 8, 9	C-7, 8, 9	
H-18	C-10, 11, 12, 15	C-10, 11, 12, 15	C-10, 15
H-19	C-11, 12, 13	C-11, 12, 13	C-11, 12, 13
H-20	C-1, 11	C-1, 11	C-1, 11, 15
OH-13			C-12, 13, 14
OH-15			C-1, 11, 15

[a] n.o.=not obserbed.
[b] H-16 and H-17 were overlapping.

The HMBC correlations between H-19/C-11, C-12, C13, H-12/C-11, C-13, C-14, C-15, H-13/C-1, C-11, C-14, and H-14/C-15 showed connections among C15–C11–C12–C13–C14–C1 (cyclohexene ring). The connection of C-18 and C-11 was confirmed by the HMBC correlations between H-18/C-11, C-12, and C-15. The connection of C-20 and C-15 was confirmed by the HMBC correlations between H-20/C-1 and C-11. The HMBC correlations from H-17 to C-7, C-8, and C-9 established the connection of C-17 and C-8, and the construction of the fragment (C5-C6-C7-C8-C9-C10). The connection of C-10 and C-11 was confirmed by the HMBC correlations between H-10/C-11, C-15, and C-18. The HMBC correlations between H-6/C-4, H-16/C-4, C-5 and H-5/C-4, C-3, C-16 established the connection of C3–C4–C5 and C-4–C-16. The HMBC correlations between H-14/C-2 and H-3/C-2 showed the construction of C1–C2–C-3. These data established the skeletal framework of **1** as consisting of a cyclohexene and a cyclododecane ring, which suggested that **1** was a phomactin derivative.[1–7] Compound **1** contains four oxygen atoms, including one carbonyl (δ_C 199.5), but also included five oxycarbons (δ_C 71.5, 64.4, 63.2, 58.9, and 55.7). Comparison of the NMR data of **1** with those of phomactin A[4] and F[2] revealed that **1** has two epoxy groups (C-3/C-4 and C-7/C-8) and one hydroxyl group at C-13. In the NOESY spectrum of **1**, NOE correlation signals were found at H_3-18/H_3-19 and H_3-19/H-13. This data suggest that H_3-18, H_3-19, and H-13 are located on the same face (Fig. 1). Single-crystal X-ray diffraction analysis was conducted to determine the absolute configuration (Fig. 2).

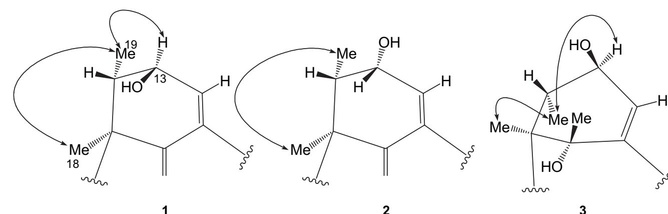


Figure 1. Selective NOESY correlations of **1**, **2** ($CDCl_3$), and **3** (DMSO-d_6).

The absolute configurations of C3, C4, C7, C8, C11, C12, and C13 were determined to be *S*, *R*, *S*, *S*, *S*, *S*, and *R*, respectively, which were deduced from the Flack parameter, −0.04 (19), refined using 1396 Friedel pairs (Fig. 2).[8]

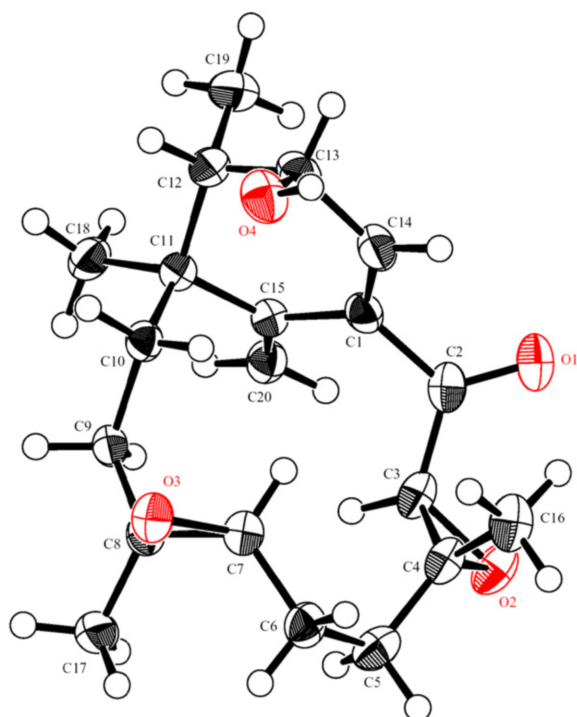


Figure 2. ORTEP drawing of **1**.

13-*epi*-Phomactin I (**2**) was obtained as a white powder. The molecular formula for **2** was determined to be $C_{20}H_{28}O_4$ (seven degrees of unsaturation) by HR-EIMS analysis (332.1982: M^+ calcd for 332.1988). The IR spectrum of **2** indicated the presence of hydroxyl (3500 cm^{-1}) and carbonyl (1700 cm^{-1}) groups. The ^{13}C NMR and DEPT data for **2** (Table 1) indicated the presence of a ketone (δ_C 198.2, C-2), four olefinic carbons (δ_C 143.7, C-15; 142.7, C-1; 132.0, C-14; 117.5, C-20), three singlet methyl carbons (δ_C 22.1, C-18; 18.9, C-17; 13.6, C-16), a doublet methyl carbon (δ_C 8.4, C-19), four methylene carbons (δ_C 35.5, C-5; 28.8, C-9; 26.3, C-10; 24.2, C-6), three oxymethine carbons (δ_C 67.6, C-13; 64.7, C-3; 55.5, C-7), a methine carbon (δ_C 44.3, C-12), two quaternary oxycarbons (δ_C 62.9, C-4; 59.1, C-8), and a quaternary carbon (δ_C 45.8, C-11). DQF-COSY and HMBC experiments (Tables 2 and 3) showed that the planar structure of **2** was the same as that of **1**. However, **2** differed from **1** in NOESY experimental results (Fig. 1). The major difference between **1** and **2** was the resonance of H-13. H_3-18 exhibited a NOESY correlation to H_3-19. Therefore **2** was an epimer of **1** at C-13.

Phomactin J (**3**) was obtained as a white powder, and crystallized as colorless prisms. The molecular formula for **3** was determined to be $C_{20}H_{30}O_5$ (six degrees of unsaturation) by HR-FABMS analysis (351.2164: $[M+H]^+$ calcd for 351.2172). The IR spectrum of **3** indicated the presence of hydroxyl (3350 cm^{-1}) and carbonyl (1700 cm^{-1}) groups. The ^{13}C NMR and DEPT data of **3** (Table 1) indicated the presence of a ketone (δ_C 199.8, C-2), two olefinic carbons (δ_C 149.5, C-1; 136.6, C-14), four singlet methyl carbons (δ_C 21.3, C-20; 19.3, C-18; 15.7 and 14.2, C-16 and C-17 may be interchanged), a doublet methyl carbon (δ_C 19.1, C-19), four methylene carbons (δ_C 39.0, C-10; 34.0, C-5; 33.8, C-9; 24.2, C-6), three oxymethine carbons (δ_C 71.4, C-13; 66.3, C-3; 60.4, C-7), a methine carbon (δ_C 42.0, C-12), three quaternary oxycarbons (δ_C 75.4, C-15; 62.8, C-4; 62.2, C-8), and a quaternary carbon (δ_C 41.2, C-11). The ^1H NMR and HMQC data (Table 1) of **3** indicated two hydroxyl groups at δ_H 5.00 (1H, d, J=5.8 Hz, OH-13) and 4.76 (1H, s, OH-15). DQF-COSY data (Table 2) and decoupling data between H-13 and H-14 of **3** showed the presence of four fragments, C-5–C-6–C-7, C-9–C-10, C-19–C-12–C-13–C-14, and C-13–OH-13. Based on these data and the HMBC correlations (Table 3), the skeleton of **3** could be established. The connection of OH-15 and C-15 was confirmed by the HMBC correlations between OH-15/C-1, C-11, and C-15. Comparison of the NMR data of **3** with those of **1** revealed that **3** has two epoxy groups at C-3/C-4 and C-7/C-8 and one hydroxyl group at C-13. The NOESY experiments for **3** (Fig.1) indicated NOE correlations of H_3-18/H_3-19 and H_3-19/H-13 suggesting that H_3-18, H_3-19, and H-13 are located on the same face (Fig. 1). Single-crystal X-ray diffraction analysis was conducted to determine the absolute configuration. The absolute configurations of C3, C4, C7, C8, C11, C12, C13, and C15 were determined to be *S*, *R*, *S*, *S*, *S*, *S*, *R*, and *R*, respectively, which were deduced from the Flack parameter, −0.01 (17), refined using 1422 Friedel pairs (Fig. 3).[8]

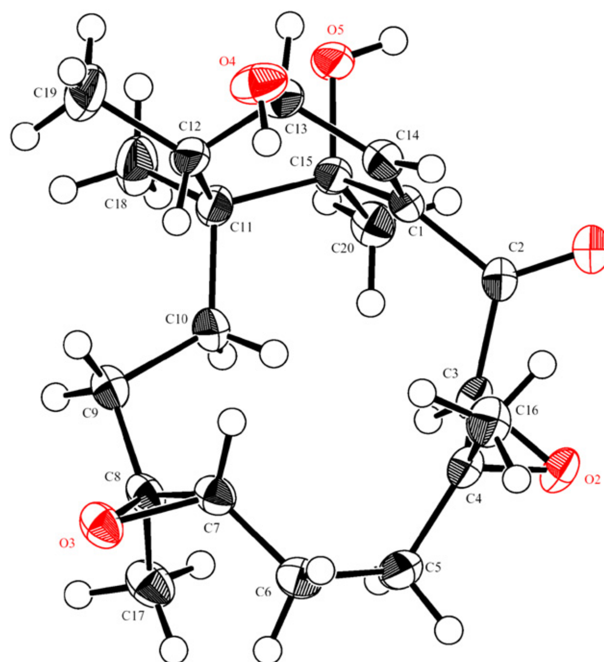


Figure 3. ORTEP drawing of **3**.

Thirteen phomactins (A,[3] B, B1, B2, C (Sch 47918[6]), D,[4] E, F, G[2] and H[1], and Sch 49026, 49027, and 49028[7]) have been isolated. Phomactins are reported to be active as platelet activating factor (PAF) antagonists.[2–5] The PAF antagonist action of phomactin I (**1**), 13-*epi*-phomactin I (**2**), and phomactin J (**3**) has not been determined, but it will be interesting to determine if they possess the activity of other phomactins.[2–5]

3. Experimental

3.1. General

Melting points were determined with a Yanagimoto MP micromelting point apparatus. UV spectra were recorded on a Shimadzu UV-240 spectrophotometer. The IR spectra were measured with a JASCO IR Report–100 infrared spectrometer. The ^1H and ^{13}C NMR spectra were recorded with JEOL JNM-AL-400 (^1H 400 and ^{13}C 100 MHz) and JEOL JNM-LA500 (^1H 500 and ^{13}C 125 MHz) spectrometers, using solvent as the internal standard. The $[\alpha]_D$ values were determined with a JASCO DIP-370 digital polarimeter and HORIBA polarimeter SEPA-300. The MS spectra were obtained using a JEOL JMS-700. Column chromatography

was carried out on 70–230 mesh silica gel (Merck) and Sephadex LH-20. HPLC was performed with a JASCO PU 980 unit and a JASCO UV 970 (Gulliver) detector using a PEGASIL Silica 60–5 (10×250 mm) column.

3.2. Extraction and isolation

Fermentation was conducted in fifty 500-mL Roux flasks, each containing 150 g wheat. Seawater (40 mL) was added to the flasks and the contents were soaked for 40 min before autoclaving for 30 min. The flasks were inoculated with the fungus (MPUC 046) and incubated at 25 °C for 31 days. The fermented wheat substrate was extracted with $CHCl_3$ (2×14 L) and EtOAc (2×14 L). The extracts of each solvent were combined, filtered, and evaporated to yield 62.57 g of crude $CHCl_3$ extract and 30.36 g of crude EtOAc extract. The $CHCl_3$ extract (62.57 g) was suspended in *n*-hexane, and this suspension separated into *n*-hexane-soluble (38.54 g) and -insoluble fractions using filtration. The insoluble fraction was suspended in MeOH, and separated further into MeOH-soluble (18.61 g) and -insoluble fractions (3.10 g) by filtration. The MeOH soluble fraction (18.61 g) was separated by silica gel column chromatography [column A; 55×170 mm; *n*-hexane/EtOAc (1:1, 1:2, 1:5, EtOAc) and $CHCl_3$/MeOH (1:1, MeOH)] into 6 fractions. Fraction A-5 (3.70 g) was separated by silica gel column chromatography [column B; 44×190 mm; $CHCl_3$/MeOH ($CHCl_3$, 100:1, 80:1, 60:1, 40:1, 10:1, MeOH)] into 3 fractions. Fraction B-1 (1.54 g) was applied to a Sephadex LH-20 column (column C; 33×450 mm; $CHCl_3$/MeOH/H_2O 6:4:1) to obtain 2 fractions. Fraction C-1 (1.11 g) was further purified by HPLC ($CHCl_3$/MeOH 100:1) to yield **1** (1.3 mg) and **2** (7.5 mg).

The EtOAc extract (30.36 g) was subjected to silica gel column chromatography [column D; 95×215 mm; *n*-hexane/$CHCl_3$ (*n*-hexane, 1:1, $CHCl_3$), $CHCl_3$/MeOH (1:1, MeOH), and $CHCl_3$/MeOH/H_2O (6:4:1)] to obtain 5 fractions. Fraction D-4 (26.22 g) was subjected to silica gel column chromatography [column E; 75×220 mm; $CHCl_3$/MeOH ($CHCl_3$, 50:1, 10:1, 1:1, MeOH)] to obtain 5 fractions. Fraction E-4 (8.51 g) was applied to a Sephadex LH-20 column [column F; 25×440 mm; $CHCl_3$/MeOH/H_2O (6:4:1)] to obtain 3 fractions. Fraction F-2 (6.08 g) was subjected to silica gel column chromatography [column G; 40×230 mm; $CHCl_3$/MeOH ($CHCl_3$, 50:1, 10:1, 1:1, MeOH)] to obtain 5 fractions. Fraction G-3 (3.15 g) was applied to a Sephadex LH-20 column [column H; 25×410 mm; $CHCl_3$/MeOH/H_2O (6:4:1)] to obtain 4 fractions. Fraction H-4 (685 mg) was applied to a Sephadex LH-20 column [column I; 25×410 mm; $CHCl_3$/MeOH/H_2O (6:4:1)] to obtain 3 fractions. Fraction I-2 (55 mg) was subjected to HPLC (column J; 10×250 mm; $CHCl_3$/MeOH 50:1) to obtain 4 fractions. Fraction J-3 (17 mg) was crystallized (*n*-hexane/$CHCl_3$/MeOH) to afford **3** (3.1 mg).

3.3. Characteristics of each diterpenoids

*3.3.1. Phomactin I (**1**).* Colorless prisms (from *n*-hexane/$CHCl_3$); mp 192–196 °C; $[\alpha]_D^{20}$ +133.6 (*c* 0.42, MeOH); UV (MeOH) λ_{max} (log ε): 220 (3.94), 258 (3.56); IR ν_{max} (KBr) cm^{-1}: 3510, 3400, 2980, 2960, 2940, 1700, 1630; HR-EIMS *m*/*z*: 332.1987 (M^+, calcd for $C_{20}H_{28}O_4$: 332.1988); EIMS *m*/*z* (rel int. %): 332 (M^+, 17), 243 (30), 163 (100), 43 (52); ^1H and ^{13}C NMR, see Table 1.

*3.3.2. 13-epi-Phomactin I (**2**).* Colorless powder; mp 189 °C; $[\alpha]_D^{20}$ +49.5 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε): 220 (3.10), 260 (2.71); IR ν_{max} (KBr) cm^{-1}: 3500, 2970, 2950, 1700, 1630; HR-EIMS *m*/*z*: 332.1982 (M^+, calcd for $C_{20}H_{28}O_4$: 332.1988); EIMS *m*/*z* (rel int. %): 332 (M^+, 17), 317 (3), 163 (100); ^1H and ^{13}C NMR, see Table 1.

*3.3.3. Phomactin J (**3**).* Colorless prisms (from *n*-hexane/$CHCl_3$/MeOH); mp 212 °C; $[\alpha]_D^{20}$ +129.4 (*c* 0.14, dioxane); UV (dioxane) λ_{max} (log ε): 213 (3.07), 239 (2.83); IR ν_{max} (KBr) cm^{-1}: 3350, 2960, 2930, 1700; positive HR-FABMS *m*/*z*: 351.2164 ($[M+H]^+$, calcd for $C_{20}H_{31}O_5$: 351.2172); FABMS *m*/*z* (rel int. %): 351 ($[M+H]^+$, 4), 333 (16), 93 (100); ^1H and ^{13}C NMR, see Table 1.

3.4. Single-crystal X-ray crystallographic analysis

All measurements were obtained using a Rigaku RAXIS RAPID Diffractometer with graphite monochromated CuKα radiation (λ=1.54187 Å). The structures of **1** and **3** were solved by direct methods (SHELX97) and expanded using Fourier techniques (DIRDIF99).

Crystal data for **1**. Colorless prismatic crystal, monoclinic, $C_{20}H_{28}O_4$ (*Mr*=332.44), space group $P2_12_12_1$ with a=8.4708(2) Å, b=13.9492(4) Å, c=15.2213(11) Å, β=95.67(5)°, V=1798.56(14) $Å^3$, Z=4, D_{calcd}=1.228 g/cm^3, R=0.0360, wR_2=0.0932, S=1.047.

Crystal data for **3**. Colorless prismatic crystal, monoclinic, $C_{20}H_{30}O_5$ (*Mr*=350.45), space group $P2_12_12_1$ with a=8.47222(10) Å, b=10.9062(2) Å, c=20.1127(14) Å, β=90°, V=1858.41(14) $Å^3$, Z=4, D_{calcd}=1.252 g/cm^3, R=0.0355, wR_2=0.0904, S=1.044.

Crystallographic data for **1** and **3** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre, under the reference numbers CCDC 763053 and 763054 respectively. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK fax: +44 1223 336033 or e-mail: data_request@ccdc.cam.ac.uk.

Acknowledgements

This work was supported by a grant from the High-Tech Research Center Project, the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan (S0801043).

References and notes

1. Koyama, K.; Ishino, M.; Takatori, K.; Sugita, T.; Kinoshita, K.; Takahashi, K. *Tetrahedron Lett.* **2004**, *45*, 6947–6948.
2. Sugano, M.; Sato, A.; Iijima, Y.; Furuya, K.; Kuwano, H.; Hata, T. *J. Antibiot.* **1995**, *48*, 1188–1190.
3. Sugano, M.; Sato, A.; Iijima, Y.; Oshima, T.; Furuya, K.; Kuwano, H.; Hata, T.; Hanazawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 5463–5464.
4. Sugano, M.; Sato, A.; Iijima, Y.; Furuya, K.; Haruyama, H.; Yoda, K.; Hata, T. *J. Org. Chem.* **1994**, *59*, 564–569.
5. Sugano, M.; Sato, A.; Saito, K.; Takaishi, S.; Matsushita, Y.; Iijima, Y. *J. Med. Chem.* **1996**, *39*, 5281–5284.
6. Chu, M.; Patel, M. G.; Gullo, V. P.; Truumees, I.; Puar, M. S. *J. Org. Chem.* **1992**, *57*, 5817–5818.
7. Chu, M.; Truumees, I.; Gunnarsson, I.; Bishop, W. R.; Kreutner, W.; Horan, A. C.; Patel, M. G.; Gullo, V. P.; Puar, M. S. *J. Antibiot.* **1993**, *46*, 554–563.
8. Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881.