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Determination of the absolute configuration of chaetoviridins and other bioactive azaphilones from the endophytic fungus *Chaetomium globosum*

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ABSTRACT

Chemical investigation of an endophytic fungus *Chaetomium globosum* isolated from leaves of *Wikstroemia uva-ursi* led to the isolation of two new azaphilones, chaetoviridins J and K (**1** and **3**), along with five known derivatives (**2** and **4**–**7**). The structures of azaphilones were determined by NMR, X-ray diffraction, Mosher's method, and CD analysis. The isolated compounds were evaluated for their cancer chemopreventive-potential based on their abilities to inhibit tumor necrosis factor alpha (TNF-α)-induced nuclear factor-kappa B (NF-κB). Compounds **4**, **5**, **7**, and synthetic **8** and **9** inhibit nitric oxide (NO) production with IC_{50} values in the range of 0.3–5.8 μM. Compounds **4**, **5**, and **9** also displayed (TNF-α)-induced NF-κB activity with IC_{50} values in the range of 0.9–5.1 μM.

Endophytes have been recognized as important sources of a variety of structurally novel active secondary metabolites with anticancer, antimicrobial, and other biological activities.[1,2] Chaetomium is the largest genera of saprophytic ascomycetes. It belongs to the Chaetomiaceae family and comprises approximately 92 species.[3] Previous investigation on secondary metabolites from the Chaetomium species resulted in the isolation of numerous types of compounds such as benzoquinone derivatives,[4] tetra-*S*-methyl derivatives,[5] azaphilones,[6,7] indol-3-yl-[13]cytochalasans,[8] and chaetoglobosin[9] analogs. In recent studies, the endophytic strain *Chaetomium globosum* isolated from the leaves of *Viguiera robusta*, was found to produce cytotoxic chaetoglobosins in Czapek medium,[9] while cytotoxic azaphilones and cytochalasan alkaloids were reported from the endophytic *C. globosum* isolated from the leaves of *Ginkgo biloba*.[10]

A crude ethyl acetate extract from the fermentation cultures of *C. globosum* found in Hawai'ian native plant, *Wikstroemia uva-ursi*, demonstrated in vitro inhibitory effects at a concentration of 20 μg/mL on the tumor necrosis factor-alpha (TNF-α)-induced NF-κB activity in transfected human embryonic kidney cells 293 cells, and lipopolysaccharide (LPS)-induced nitric oxide production using murine macrophage RAW 264.7 cells. Bioassay-guided fractionation of this extract resulted in the isolation of two new chaetoviridins J and K (**1** and **3**), together with five known compounds **2** and **4**–**7**. Two chaetomugilins E and F (**8** and **9**) were obtained from **2** (Fig. 1). This paper reports the isolation and structure elucidation of the new chaetoviridins and the biological activity.

Compound **1**[11] was obtained as a yellow amorphous powder and gave a molecular ion at *m*/*z* 431.1499 $[M+Na]^+$ (Calcd for $C_{22}H_{29}ClO_5Na$, 431.1435) in the positive-ion HRESIMS, corresponding to a molecular formula of $C_{22}H_{29}ClO_5$. The ratio of isotope peak intensities (MH^+/$[MH+2]^+$) supports one chlorine atom. The UV spectrum showed absorption bands at 255, 297, 388 nm indicating a highly conjugated system. The IR spectrum exhibited bands at 3350, 1700 cm^{-1}, characteristic of a hydroxyl and an α,β-unsaturated carbonyl functionalities, respectively. The NMR (Table 1), HSQC, and HMBC spectra revealed the presence of a number of olefinic groups; trisubstituted two olefinic groups at [δ_H 7.44/δ_C 145.3 (C-1) and 119.5 (C-8a) and δ_H 6.46/δ_C 104.4 (C-4) and 157.3 (C-3)], a *trans*-olefinic group at [δ_H 6.51 (dd, J = 15.6, 8.0 Hz)/δ_C 146.3 (C-10) and δ_H 6.03 (d, J = 15.6 Hz)/δ_C 120.2 (C-9)] due to large coupling constants, one quaternary olefinic carbon at δ_C 141.7 (C-4a), and an upfield shifted olefinic quaternary carbon (δ_C 106.6) indicating the

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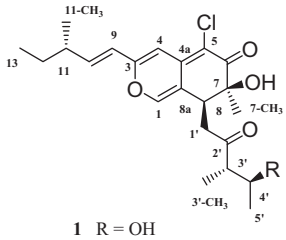
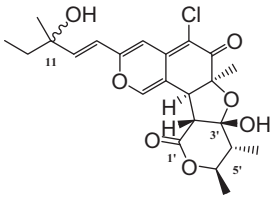
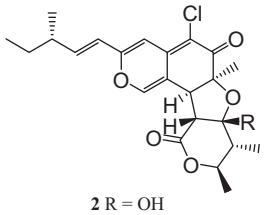


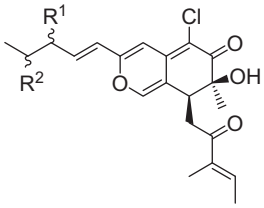
1 R = OH
1a R = O(*R*)-MTPA
1b R = O(*S*)-MTPA



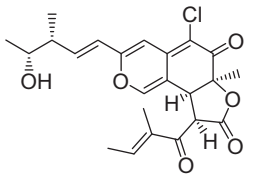
3 (11*R* and 11*S*)



2 R = OH
8 R = OCH_3



4 $R^1 = \beta CH_3$, $R^2 = \alpha OH$
5 $R^1 = \alpha CH_3$, $R^2 = \alpha OH$
7 $R^1 = \alpha CH_3$, $R^2 =$ H



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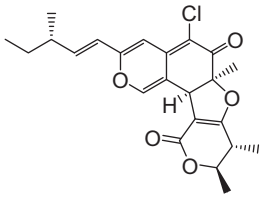

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Figure 1. Chemical structures of compounds **1**–**9**.

attachment of a chlorine atom at C-5.[12] All of the olefinic groups were confirmed to be closely connected to each other through the HMBC analysis (Fig. 2), which indicated a typical conjugation system of the azaphilones.[6,12,13]

The ^{1}H and ^{13}C NMR spectra (Table 1) revealed additional signals for three aliphatic secondary methyls (11-CH_3, 3′-CH_3, and CH_3-5′), a tertiary methyl (7′-CH_3), a terminal ethyl (C-12–C-13), a methylene (C-1′), three methines (C-11, C-8, and C-3′), an oxygen-bearing methine (C-4′), an oxygenated quaternary carbon (C-7), and two carbonyl carbons (C-6 and C-2′), which were almost identical with chaetomugilin J (**7**) (Fig. S32, Supplementary data),[14] except for the oxygenated methine group (C-4′) replacing the olefinic double bond (C-3′–C-4′) in **7**. The HMBC correlations between H-4′ and C-2′/3′-CH_3/CH_3-5′ supported the position of the oxymethine group (Fig. 2). The absolute stereochemistry at C-7 of azaphilones has been established as *S* by circular dichroism (CD) and X-ray analyses.[6,13,15] The absolute configuration at C-7 of **1** was also determined as *S* by comparison of the CD spectrum (Fig. 6).[12] The NOESY spectrum of **1** showed a correlation between H-8 and 7-CH_3, implying that H-8 is oriented as *cis* to the 7-CH_3 group (Fig. S5, Supplementary data). The modified Mosher's method was applied to determine the absolute stereochemistry of the secondary hydroxy group at C-4′. Esterification of **1** with (*R*)- or (*S*)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (MTPA-Cl) gave bis (*R*)- and (*S*)-MTPA esters, **1a** and **1b**, respectively, (Fig. 3).

A negative $\Delta\delta^{SR}$ value for proton CH_3-5′ and positive values for H-1′, H-3′, and 3′-CH_3 were observed in the ^{1}H NMR spectra of **1a** and **1b**, which established the absolute configuration at C-4′ as *S*. The stereochemistry at C-11 and C-3′ was determined as *S* by comparison of NMR data with previously published value.[6,12–14] These evidences allowed assignment of the configuration of the

Table 1
^{1}H and ^{13}C NMR spectroscopic data of compounds **1**–**3**

Position	**1**[a]		**2**[a]		**3**[a]		**2** (in DMSO-d_6)
	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)	δ_C	δ_H, mult. (*J* in Hz)
1	7.44 s	145.3	7.29 s	146.8	7.30 s	145.7	7.49 s
2							
3		157.3		157.7		157.2	
4	6.46 s	104.4	6.56 s	104.9	6.64 s	106.1	6.67 s
4a		141.7		140.3		140.1	
5		106.6		110.1		110.5	
6		191.6		189.2		189.3	
7		74.1		83.9		83.9	
8	3.47 dd (9.6, 3.2)	39.9	3.00 d (10.0)	50.5	3.00 d (10.0)	50.0	3.39[b]
8a		119.5		114.3		114.3	
9	6.03 d (15.6)	120.2	6.07 d (15.6)	120.1	6.39 d (15.6)	119.2	6.39 d (16.0)
10	6.51 dd (15.6, 8.0)	146.3	6.51 dd (15.6, 8.4)	145.5	6.63 d (15.6)	145.5	6.50 dd (16.0, 7.6)
11	2.26 m	38.7	2.27 m	38.8		73.5	2.26 m
12	1.44 m	29.2	1.44 m	29.1	1.66 q (7.6)	35.0	1.40 m
13	0.91 t (7.4)	11.6	0.91 t (7.6)	11.6	0.94 t (7.6)	8.1	0.86 t (7.6)
7-CH_3	1.32 s	26.6	1.41 s	23.4	1.42 s	23.2	1.23 s
11-CH_3	1.09 d (6.8)	19.3	1.09 d (6.4)	19.4	1.38 s	27.7	1.04 d (6.8)
1′a	3.22 dd (18.4, 3.2)	40.6		170.6		170.5	
1′b	2.40 dd (18.4, 9.6)						
2′		213.7	3.08 d (10.0)	58.2	3.08 d (10.0)	58.2	2.72 d (10.8)
3′	2.43 dq (7.6, 7.2)	54.0		104.1		104.1	
4′	3.87 dq (7.6, 6.4)	69.7	1.90 dq (10.0,6.6)	44.9	1.90 m	44.9	1.69 dq (10.2,6.8)
5′	1.14 d (6.4)	20.9	4.31 dq (10.0,6.6)	77.2	4.32 m	77.2	4.31 dq (10.2,6.4)
6′			1.43 d (6.6)	18.8	1.43 d (6.8)	18.9	1.28 d (6.4)
3′-CH_3	1.05 d (7.2)	13.7					
4′-CH_3			1.15 d (6.6)	8.7	1.15 d (6.8)	8.7	1.01 d (6.8)
3′-OH							6.31 s

[a] Spectra recorded at ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) in $CDCl_3$. Chemical shift (δ) are in ppm, and coupling constants (*J* in Hz) are given in parentheses. The assignments were based on DEPT, COSY, NOESY, HSQC, and HMBC experiments.

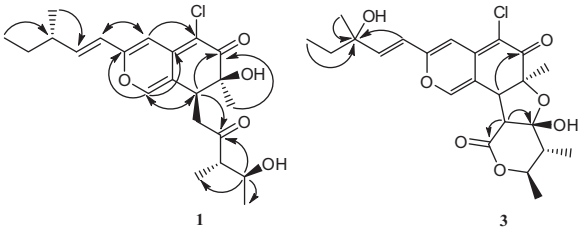

Figure 2. Important HMBC correlations for compounds **1** and **3**.

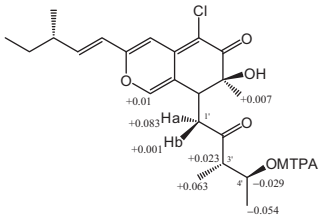

Figure 3. ^{1}H chemical-shift difference ($\Delta\delta = \delta_S - \delta_R$) between the (*R*)- and (*S*)-MTPA esters (**1a** and **1b**).

asymmetric carbons (7*S*, 8*S*, 11*S*, 3′*S*, and 4′*S*), and has been named chaetoviridin J.

Compound **2**[16] was obtained as a yellow amorphous powder and its MS and NMR spectra were in good agreement with those of the known compound, chaetomugilin D (Fig. 1);[6,12] the structure was further confirmed by HSQC and HMBC analyses. The stereochemistry of **2** was established from its CD and NOESY correlations of H-2′ with H-4′/4′-CH_3 and of H-5′ with H-8/7-CH_3 (Fig. 4), along with the comparison of those of synthetic, chaetomugilin E (**8**) and chaetomugilin F (**9**) (Scheme S1).[12,17,18]

In addition, the absolute configuration of **2** was supported by means of X-ray crystallographic analysis through its chemical derivatization. The treatment of **2** with *p*-bromobenzoic acid in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) gave the *p*-bromobenzoate ester **2a**, where attached to C-7 and C-3′ positions derived from **2**,[19] as shown in Scheme S2 (Supplementary data), revealing the chemical conversion and its stereochemistry.[12,14]

This chemical transformation facilitated the determination of the absolute stereochemistry of the asymmetric positions through X-ray crystallographic analysis (Fig. 5).

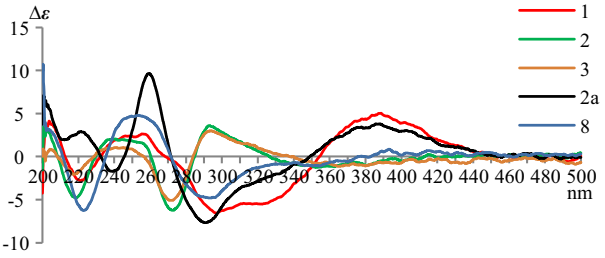

Figure 6. CD spectra of **1**–**3**, **2a**, and **8**.

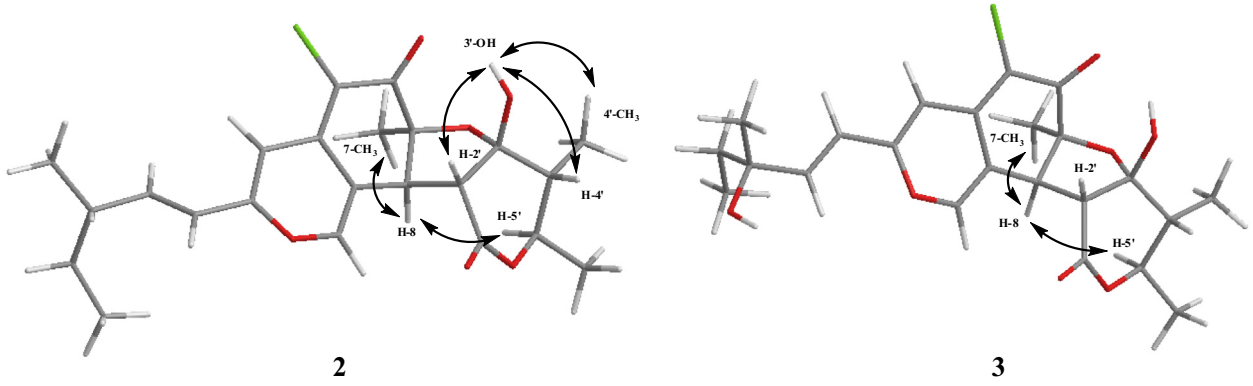

Figure 4. Key NOESY correlations for compounds **2** and **3**.

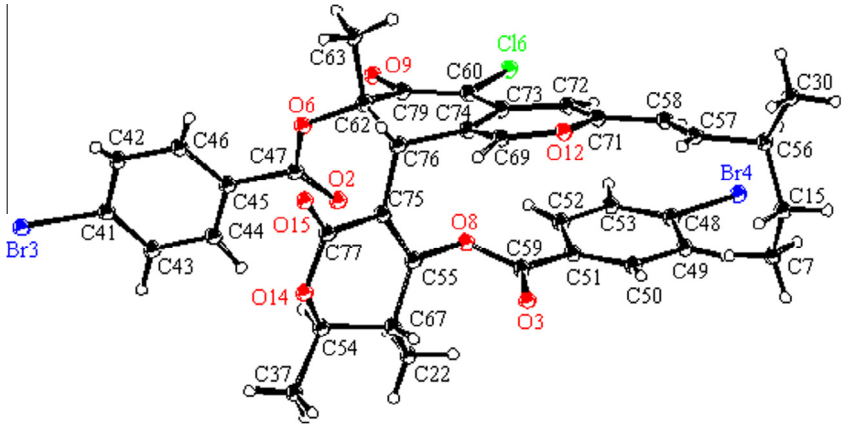

Figure 5. ORTEP drawing of one of the two crystallographically independent molecules in the unit cell of compound **2a**; displacement ellipsoids are drawn at the 50% probability level at 90K.

Table 2
Inhibition effect of compounds **1**–**5** and **7**–**9** against the TNF-α-induced NF-κB activity and NO production in LPS-stimulated RAW 264.7 cells

Compounds	NF-κB			Nitrite assay (NO)			
	% Inhib.[a]	% Surv.[b]	IC_{50} (μM)	% Inhib.[c]	% Surv.[d]	IC_{50} (μM)	Cytotoxicity (IC_{50} μM)
1	32.6 ± 5.0	100 ± 12.3	nd[e]	95.4 ± 2.0	71.1 ± 4.0	nd	
2	28.2 ± 0.9	100 ± 15.8	nd	68.2 ± 1.9	85.3 ± 2.3	28.1 ± 4.1	
3	33.4 ± 2.5	100 ± 8.9	nd	39.4 ± 2.9	95.7 ± 2.1	nd	
4	99.9 ± 0.1	100 ± 11.0	0.9 ± 0.2	99.6 ± 0.4	32.9 ± 1.3	0.8 ± 0.7	6.8 ± 1.4
5	99.9 ± 0.2	59.2 ± 12.0	0.9 ± 0.2	99.9 ± 0.2	37.1 ± 1.5	0.3 ± 0.1	1.5 ± 0.1
7	74.2 ± 1.9	83.4 ± 6.2	7.6 ± 1.4	99.9 ± 2.1	36.2 ± 5.6	4.2 ± 0.9	4.2 ± 0.9
8	88.5 ± 3.8	100 ± 16.4	11.6 ± 2.1	97.9 ± 0.7	28.0 ± 6.1	5.8 ± 0.6	39.8 ± 5.8
9	97.7 ± 3.1	82.8 ± 3.3	5.1 ± 1.9	99.3 ± 0.2	28.5 ± 1.0	1.9 ± 0.1	20.7 ± 1.0
L-NMMA[f]						25.1 ± 2.3	
TPCK[g]			3.8 ± 0.6				
BAY-11[g]			2.0 ± 0.3				

Assays were conducted in triplicate, and the each result is expressed as the average ± standard deviation.
[a] % Inhibition of NO production at 50 μM.
[b] % cell survival at concentration of 50 μM.
[c] % Inhibition of NF-κB at 50 μM.
[d] % Survival at concentration of 50 μM.
[e] nd, not determined.
[f] Positive control for NO.
[g] Positive control for NF-κB.

Compound **3**[20] was obtained as a white amorphous powder and its molecular formula was established as $C_{23}H_{27}ClO_7$ by HRESIMS (observed, 473.1350; Calcd for $[M+Na]^+$ 473.1338), corresponding to a molecular formula of $C_{23}H_{27}ClO_7Na$. The ratio of isotope peak intensities ($MH^+/[MH+2]^+$) indicated one chlorine atom was present. The ^1H and ^{13}C NMR spectra displayed highly conjugated olefinic system, four methyls, and three methines, including an oxygenated methine, a methylene, an ester carbonyl carbon, a conjugated carbonyl carbon, an oxygenated quaternary carbon, and a hemiacetal carbon, closely resembled to those of **2**. However, the NMR spectra of **3** showed additional signals for a quaternary methyl group at δ_H 1.38 (3H, s)/δ_C 27.7 (11-CH_3), an oxygenated quaternary carbon at δ_C 73.5 (C-11), and a *trans*-doublet olefinic proton at δ_H 6.63 (d, J = 15.6 Hz, H-10), instead of the doublet methyl (11-CH_3), the methine group (H-11), and the *trans*-double doublet olefinic proton (H-10) in the 3-(3-methyl-1-pentenyl) moiety of **2**. The HMBC correlations between 11-CH_3/CH_3-13/H-10 and the oxygenated quaternary carbon (C-11), along with the HRESIMS analysis suggested that a hydroxyl group was attached at C-11 position (Fig. 2). Two sets of the NMR signals corresponding to the side chain, 3-(3-methylpent-1-en-3-ol) group indicated that **3** was, in fact, a mixture of unresolvable diastereoisomer. The attempts at purification of this mixture by chiral columns were unsuccessful. The configuration of asymmetric centers except for C-11 in **3** was determined to be the same with those of chaetomugilin D (**2**) and its derivative **2a**, as shown in Scheme S2, by comparison of their NMR and NOESY spectra (Table 1 and Figs. 4 and S17), along with physicochemical analyses,[6,13,15] and has been named chaetoviridin K.

The other four isolates were identified as the known compounds, 11-*epi*-chaetomugilin I (**4**),[12] chaetomugilin I (**5**),[12] chaetomugilin N (**6**),[14] and chaetomugilin J (**7**),[14] along with the derivatives of **2**, namely, chaetomugilins E (**8**) and F (**9**),[17,18] by comparison of their physical and spectral data with published values.

Compounds **1**–**5**, **7**, and the chaetomugilins E and F (**8** and **9**) were subsequently evaluated for their cancer chemopreventive potential based on their ability to inhibit tumor necrosis factor alpha (TNF-α)-induced NF-κB activity and nitric oxide (NO) production (Table 2). Among tested compounds, **4** and **5** inhibited TNF-α-induced NF-κB activity with the same IC_{50} value of 0.9 μM, but **4** showed no cytotoxicity at a concentration at 50 μM. Compounds **7**–**9** showed moderate inhibitory activity with IC_{50} values ranging from 5.1 to 11.6 μM. The NO inhibitory activity of these compounds was initially evaluated at a fixed concentration at 50 μM. Compounds **1**, **4**, **5**, and **7**–**9** exhibited strong inhibitory activity against NO production (95.4–99.9%). Among them, compounds **4** and **5** inhibited NO release, with IC_{50} values of 0.8 ± 0.7 and 0.3 ± 0.1 μM, respectively, which demonstrated more potency than the positive control, *N*-monomethyl-L-arginine (25.1 μM). However, cytotoxicity of both compounds was observed at 50 μM. Compounds **7**–**9** also showed considerable inhibitory activity with IC_{50} values ranging from 1.9 to 5.8 μM, while compound **3** exhibited a weak response.

Acknowledgments

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Supplementary data

The X-ray crystallography data of compound **2a** in this Letter has been deposited with the Cambridge Crystallography Data Center as supplementary publications No. CCDC1025151-102515. The data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bmcl.2015.08.063.

References and notes

1. Krohn, K.; Kock, I.; Elsässer, B.; Flörke, U.; Schulz, B.; Draeger, S.; Antus, S.; Kurtán, T. *Eur. J. Org. Chem.* **2007**, *7*, 1123.
2. Strobel, G.; Daisy, B.; Castillo, U.; Harper, J. *J. Nat. Prod.* **2004**, *67*, 257.
3. Von Arx, J. A.; Guarro, J.; Figueras, M. J. *Nova Hedwigia* **1986**, *84*, 1.
4. Brewer, D.; Jerram, W. A.; Taylor, A. *Can. J. Microbiol.* **1968**, *14*, 861.
5. Safe, S.; Taylor, A. *J. Chem. Soc. Perkin Trans. 1* **1972**, 472.
6. Takahashi, M.; Koyama, K.; Natori, S. *Chem. Pharm. Bull.* **1990**, *38*, 625.
7. Kanokmedhakul, S.; Kanokmedhakul, K.; Nasomjai, P.; Soytong, K.; Isobe, M.; Kongsaeree, P.; Prabpai, S.; Suksamrarn, A. *J. Nat. Prod.* **2006**, *69*, 891.

8. Silverton, J. V.; Akiyama, T.; Kabuto, C.; Sekita, S.; Yoshihira, K.; Natori, S. *Tetrahedron Lett.* **1976**, *17*, 1349.
9. Momesso, L. S.; Kawano, C. Y.; Ribeiro, P. H.; Namizo, A.; Goldman, G. H.; Pupo, M. T. *Quim. Nova* **2008**, *31*, 1680.
10. Qin, J.-C.; Zhang, Y.-M.; Gao, J.-M.; Bai, M.-S.; Yang, S.-X.; Laatsch, H.; Zhang, A.-L. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1572.
11. Chaetoviridin J (**1**): yellow amorphous powder; $[\alpha]_D^{20}$ = +130° (*c* 0.2, MeOH); UV (MeOH) λ_{max} (log ε) 292 (2.6), 386 (4.5), 407 (4.0) nm; CD (*c* 0.1, MeOH) 255 (+2.6), 297 (−6.5), 388 (+2.6); IR ν_{max} (KBr) 3350, 1700 cm^{-1}; ^1H (400 MHz) and ^{13}C NMR (100 MHz) data, see Table 1; HRESIMS *m*/*z* 431.1499 $[M+Na]^+$ (Calcd for $C_{22}H_{29}ClO_5Na$, 431.1435).
12. Yamada, T.; Muroga, Y.; Jinno, M.; Kajimoto, T.; Usami, Y.; Numata, A.; Tanaka, R. *Bioorg. Med. Chem.* **2011**, *19*, 4106.
13. Borges, W. S.; Mancilla, G.; Guimaraes, D. O.; Duran-Patron, R.; Collado, I. G.; Pupo, M. T. *J. Nat. Prod.* **2011**, *74*, 1182.
14. Muroga, Y.; Yamada, T.; Numata, A.; Tanaka, R. *Tetrahedron* **2009**, *65*, 7580.
15. Steyn, P. S.; Vleggaar, R. *J. Chem. Soc. Perkin Trans. 1* **1976**, 204.
16. Chaetomugilin D (**2**): yellow amorphous powder; $[\alpha]_D^{10}$ = +140° (*c* 0.05, MeOH); UV (MeOH) λ_{max} (log ε) 284 (3.5), 385 (4.2), 405 (4.5) nm; CD (*c* 0.1, MeOH) 240 (+2.0), 272 (−6.2), 293 (+3.5); IR ν_{max} (KBr) 3340, 1765 cm^{-1}; ^1H (400 MHz) and ^{13}C NMR (100 MHz) data, see Table 1; HRESIMS *m*/*z* 435.1577 $[M+H]^+$ (Calcd for $C_{23}H_{28}ClO_6$, 435.1569).
17. Yasuhide, M.; Yamada, T.; Numata, A.; Tanaka, R. *J. Antibiot.* **2008**, *61*, 615.
18. Yamada, T.; Doi, M.; Shigeta, H.; Muroga, Y.; Hosoe, S.; Numata, A.; Tanaka, R. *Tetrahedron Lett.* **2008**, *49*, 4192.
19. Compound (**2a**): yellow crystal; $[\alpha]_D^{20}$ = +220° (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 252 (4.0), 387 (3.2), 403 (3.0) nm; CD (*c* 0.1, MeOH) 255 (+2.6), 297 (−6.5), 388 (+2.6); ^1H (400 MHz) and ^{13}C NMR (100 MHz) data, see Figures S17 and S18.
20. Chaetoviridin K (**3**): yellow amorphous powder; $[\alpha]_D^{20}$ = +360° (*c* 0.025, MeOH); UV (MeOH) λ_{max} (log ε) 254 (4.0), 388 (3.0), 405 (3.2) nm; CD (*c* 0.1, MeOH) 244 (+1.0), 271 (−5.0), 293 (+2.99); ^1H (400 MHz) and ^{13}C NMR (100 MHz) data, see Table 1; HRESIMS *m*/*z* 473.1350 $[M+Na]^+$ (Calcd for $C_{23}H_{27}ClO_7Na$, 473.1338).