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Angumycinones A and B, two new angucyclic quinones from *Streptomyces* sp. KMC004 isolated from acidic mine drainage ☆

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ABSTRACT

Two new angucyclic quinones, angumycinones A (**1**) and B (**2**) and six known angucyclinone analogues (**3**–**8**) were isolated from a liquid culture extract of the *Streptomyces* sp. KMC004 strain from acidic coal mine drainage. The structures of these compounds were established using extensive spectroscopic data analyses, including NMR, HRFABMS, UV, CD, and X-ray crystallography. Compounds **1**–**8** were tested for antimicrobial activity against ten pathogenic microbial or fungal strains. Angumycinone B (**2**) exhibited antimicrobial activity against *Micrococcus luteus*, *Enterococcus hirae*, and methicillin-resistant *Staphylococcus aureus* (MRSA) with minimum inhibitory concentration values of 0.78, 1.56, and 12.5 μg/mL, respectively.

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Microorganisms are a fertile resource for natural product-based drug discovery programs. In particular, terrestrial soil-derived *Streptomyces* species have been extensively studied because they can potentially provide pharmaceutical candidates; approximately 70% of clinically useful antibiotics are derived from natural sources.[1] However, the chemical redundancy of products isolated from these bacteria has become one of the current challenges in the discovery of novel natural product-derived drug candidates.[2] One approach to overcome this problem is to utilize *Streptomyces* species derived from unique habitats, such as marine environments,[3] mutualistic associations with hosts,[4] etc.; these strains have been exploited to provide novel microbial chemotypes over the last few years. Many recent investigations have uncovered compelling evidence that the *Streptomyces* species derived from unique environmental samples might lead to the discovery of secondary metabolites with significant biological activity.[5]

Acidic mine drainage is generated by the oxidative reactions that result from the exposure of sulfide minerals, such as iron pyrite or iron disulfide, to the atmosphere. Acidic mine drainage is a geochemically extreme environment,[6] and the acidic water system provides ecologically unique habitats for the growth and metabolism of diverse microbes.[7] Under harsh environmental conditions, such as acidic mine drainage, microorganisms may face ecological competition, driving their metabolic potential and requiring the biosynthesis of new secondary metabolites.[8]

The *Streptomyces* sp. KMC004 strain was isolated from an acidic mine drainage sample (209 ppm Fe, 6.7 ppm Mn, 0.8 ppm Pb, and 0.8 ppm Cu; pH 3.0) collected from the Young-dong abandoned coal mine located at Gangneung, South Korea, during our ongoing investigation of novel secondary metabolites from microorganisms collected from unique environments. The strain was most likely a *Streptomyces* sp. based on the 98.3% 16S rRNA sequence similarity with the *Streptomyces chryseus* strain (EU841613). The *Streptomyces* sp. KMC004 strain was cultivated in YM liquid medium (5 g of yeast and 30 g of malt in 1 L of distilled water) for 10 days at 25 °C. The initial high-performance liquid chromatography mass spectrometry (HPLC/MS) analyses of the liquid cultured KMC004 revealed six major constituents with characteristic quinone-like ultraviolet (UV) chromophores.[9] To identify their molecular structures, the whole culture broth (8 L) was extracted with ethyl acetate (16 L), and the extracts (1.2 g) were subjected to gradient reverse-phase chromatography. The six major metabolites were identified as known angucyclinone structures [MM 47755 (**3**),[10] (+)-rubiginone B_2 (**4**),[11] (+)-ochromycinone (**5**),[12] (+)-hatomarubigin A (**6**),[13] (+)-rubiginone D_2 (**7**),[14] and X-14881 E (**8**)[15] by comparing their spectroscopic data with previously reported spectroscopic data (Fig. 1). Angucyclinones are characterized with an angular tetracyclic (benz[*a*]anthracene) carbon skeleton and are one of the many aromatic polyketides predominantly isolated from

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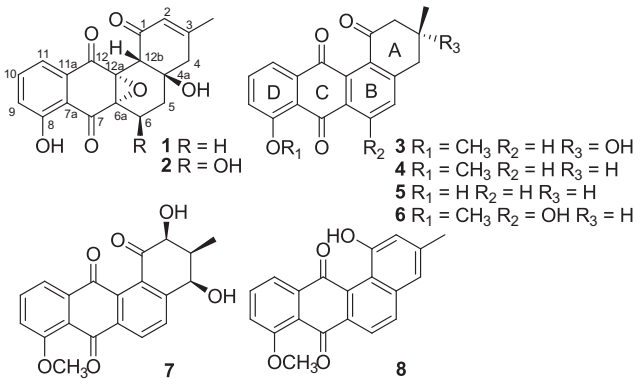

Figure 1. Structures of compounds **1**–**8**.

soil-derived *Streptomyces* spp.[16] Most of the previously reported angucyclinone analogues have exhibited a broad range of biological properties, including cytotoxicity,[17] antibacterial,[18] and platelet aggregation inhibition properties.[19] To date, angucyclic quinones are continuously growing more attractive as a class of natural products due to their structural diversity, biomedical potential, and well-defined biosynthetic pathways.[16,20] Therefore, we investigated the liquid culture media of KMC004 further to discover novel angucyclic quinones. Consequently, two highly oxygenated angucyclic quinones (Fig. 1) were isolated as minor constituents (**1**: 8 mg and **2**: 5 mg) from ethyl acetate extracts (1.2 g) of *Streptomyces* sp. KMC004 strain and named angumycinones A (**1**) and B (**2**). Herein, we describe the isolation, structure elucidation, and antimicrobial activities of **1** and **2**.

Angumycinone A (**1**)[21] was obtained as colorless block crystal with an assigned molecular formula of $C_{19}H_{16}O_6$ based on our high resolution fast-atom bombardment mass spectrometry (HRFABMS) data (obsd $[M+H]^+$ *m/z* 341.1025, calcd 341.1025). The infrared (IR) spectrum of **1** displayed intense absorption bands at 3427 and 1640 cm^{-1}, suggesting the presence of hydroxyl and carbonyl groups, respectively. The UV spectrum of **1** revealed a quinone-like chromophore.[9] The ^1H NMR spectrum was recorded in pyridine-d_5 and displayed signals for three aromatic methines (δ_H 7.54, 7.43, and 7.21), a vinyl methine (δ_H 5.95), a methine (δ_H 4.56), three methylene groups [(δ_H 3.03, 2.49), (δ_H 3.00, 2.46), and (δ_H 1.84, 1.58)], a methyl (δ_H 1.76), and two exchangeable protons (δ_H 11.63 and 7.03). The ^{13}C NMR spectrum revealed 19 signals, including three aromatic methine carbons (δ_C 136.8, 123.5, and 119.6), one vinyl methine carbon (δ_C 125.5), three aromatic quaternary carbons (δ_C 161.1, 133.6, and 115.4), a vinyl quaternary carbon (δ_C 159.6), three carbonyl carbons (δ_C 197.9, 194.8, and 192.2), three oxygenated quaternary carbons (δ_C 68.7, 66.1, and 64.4), three methylene carbons (δ_C 46.2, 27.2, and 18.1), one methine carbon (δ_C 49.9), and a methyl carbon (δ_C 24.0). Analyses of the ^1H and ^{13}C NMR spectral data indicated that the compounds had characteristics of the tetracyclic benz[*a*]anthracene class, referring to an angularly constructed framework composed of four conjugated ring systems (rings A–D) (Table 1).[16] Analyses of the extensive 2D NMR spectral data led to the identification of the planar structure of compound **1** (Fig. 2). The COSY correlations from both H-11 at δ_H 7.54 and H-9 at δ_H 7.21 (dd, J = 8.5, 1.5 Hz) to H-10 (δ_H 7.43, dd, J = 8.5, 7.5 Hz) suggested the presence of 1,2,3-trisubstituted benzene ring (D-ring). The aromatic methine H-10 (δ_H 7.43) exhibited a HMBC correlation to the oxygenated aromatic quaternary carbon C-8 (δ_C 161.1), and the phenolic OH signal attached at C-8 displayed a downfield shifted proton resonance (δ_H 11.63) due to intramolecular hydrogen-bonding with the adjacent carbonyl C-7 (δ_C 197.9).[22] An additional COSY correlation between two methylene groups [H_2-5 (δ_H 1.84 and 1.58) and H_2-6 (δ_H 3.00 and 2.46)], coupled with HMBC correlations from methylene H_2-6 to C-4a (δ_C 68.7), C-6a (δ_C 66.1), and C-12a (δ_C 64.4), and from another methylene H_2-5 to C-4a (δ_C 68.7) and C-6a (δ_C 66.1), allowed us to construct the B-ring and assign its substituted pattern (Fig. 1). In addition, the construction of the A-ring was established with the HMBC correlations from the vinyl methine H-2 (δ_H 5.95) to C-4 (δ_C 46.2) and from a methyl singlet (δ_H 1.76) to C-2 (δ_C 125.5) and C-3 (δ_C 159.6), indicating the presence of a methyl-substituted double bond.[23] The connectivity of the A- and B-rings was achieved based on the HMBC correlations from H-2, H-4, and H_2-5 to C-12b (δ_C 49.9) and from H-4 to C-5 (δ_C 27.2). Finally, the planar structure of **1** was determined using the HMBC correlations from H-11 and H-12b to C-12 (δ_C 192.2), in addition to the weak HMBC correlation between H-11 and C-7 (δ_C 197.9), suggesting that the C-ring was quinone-like. The existence of an epoxide between C-6a (δ_C 66.1) and C-12a (δ_C 64.4) was deduced by comparing the ^{13}C chemical shifts with the spectra data of previously reported compounds.[24]

The relative configuration of H-12b was initially determined by interpreting the 2D NOESY NMR spectral data and long range correlation between H-12b and H-5β in the ^1H–^1H COSY spectrum of **1**. The strong NOE correlation between the methine H-12b and H-4β indicated that these two protons were axially placed on the same side. The methane H-12b demonstrated a ^1H–^1H COSY correlation with H-5β, indicating the W-shape arrangement of the connecting bonds between H-12b and H-5β. This alignment was also supported by long range coupling ($^4J_{12b,5\beta}$ = 2.0 Hz) between H-12b and H-5β proton signals in the ^1H NMR spectrum of **1**.[25] These data allowed us to assign the relative configuration of H-12b and H-5β to be *cis*-configuration. The absolute configuration of **1** was deduced with a direct method to be 4a*R*, 6a*S*, 12a*R*, and 12b*R* via single crystal X-ray diffraction analyses conducted with Mo Kα radiation, resulting in a refined Flack parameter value of 1.2(9) using 1553 Friedel pairs (Fig. 3).[26]

Angumycinone B (**2**)[27] was obtained as pale yellowish oil. An HRFABMS analysis indicated that the molecular formula of **2** was $C_{19}H_{16}O_7$ (obsd $[M+H]^+$ *m/z* 357. 0980, calcd 357.0974). The ^1H and ^{13}C NMR spectral data of **2** were very similar to that of **1**; the major differences between the two data sets were signals indicating the presence of the additional hydroxyl group (δ_H 8.10) and an oxygenated methine (δ_H 5.23, δ_C 62.7),[28] suggesting that **2** was a 6-hydroxy analogue of **1**. The attachment of the hydroxyl group at C-6 in **2** was confirmed by the COSY correlations of both H_2-5 (δ_H 2.08 and 1.93) and 6-OH (δ_H 8.10) with H-6 (δ_H 5.23) and the HMBC correlation from H_2-5 to C-6 (δ_C 62.7). The relative and absolute configurations of **2** were assigned by analyzing the NOESY correlations together with CD spectral data. The CD and NOESY spectra of **2** were very similar to that of **1**. The broad singlet signal of H-6 in the ^1H NMR spectrum of **2** and the key NOESY correlations of both axial H-5α and equatorial H-5β with H-6 suggested that the 6-OH was placed axially in the β-orientation, while H-6 was in an α-equatorial configuration. In addition, the methane H-12b demonstrated a long range correlation ($^4J_{12b,5\beta}$ = 2.3 Hz) with H-5β in the ^1H–^1H COSY and ^1H NMR spectra of **2**, indicating W-shape connection and *cis*-configuration of H-12b and H-5β. The absolute configuration of **2** was determined to be 4a*S*, 6*R*, 6a*S*, 12a*R*, and 12b*R* and was validated with the very similar CD spectra of **2** and **1** (Fig. 4).

The angumycinones (**1** and **2**) represent highly oxygenated angucyclic quinones; this scaffold is characterized by the presence of an epoxide group situated between C-6a and C-12a. Only nine natural 6a,12a-epoxybenz[*a*]anthracene derivatives have been reported so far from soil-based *Streptomyces* species.[9,14,23,24,28,29] Of these nine structures, angumycinone A (**1**) is the most similar in structure to grecocycline A aglycon, which features a hydroxyl group positioned at C-12b. One critical difference in structure

Table 1
^{1}H and ^{13}C NMR spectral data for compounds **1** and **2** in pyridine-d_5 (δ_H 8.69, δ_C 149.9)

	Compound **1**			Compound **2**		
Position	δ_H mult (*J*, Hz)[a]	δ_C[b]		δ_H mult (*J*, Hz)[a]	δ_C[b]	
1		194.8	C		194.6	C
2	5.95 s	125.5	CH	5.93 dd (2.0, 1.0)	125.6	CH
3		159.6	C		159.7	C
3-CH_3	1.76 br s	24.0	CH_3	1.75 br s	24.0	CH_3
4_β	3.03[c]	46.2	CH_2	2.91 ddd (18.0, 2.5, 1.0)	45.7	CH_2
4_α	2.49 d (17.0)			2.47 d (18.0)		
4a		68.7	C		71.1	C
5_α	1.84 ddd (18.0, 13.0, 5.0)	27.2	CH_2	2.08 dd (14.5, 3.5)	34.8	CH_2
5_β	1.58 m			1.93 ddd (14.5, 2.5, 2.3)		
6_β	3.00[c]	18.1	CH_2			
6_α	2.46 dd (13.0, 5.0)			5.23 br s	62.7	CH
6a		66.1	C		66.4	C
7		197.9	C		196.3	C
7a		115.4	C		115.3	C
8		161.1	C		162.0	C
9	7.21 dd (8.5, 1.5)	123.5	CH	7.22 dd (8.5, 1.0)	124.2	CH
10	7.43 dd (8.5, 7.5)	136.8	CH	7.45 dd (8.5, 7.5)	137.3	CH
11	7.54[c]	119.6	CH	7.56 dd (7.5, 1.0)	120.0	CH
11a		133.6	C		133.0	C
12		192.2	C		191.0	C
12a		64.4	C		64.7	C
12b	4.56 d (2.0)	49.9	CH	4.66 d (2.3)	51.1	CH
4a-OH	7.03			7.43		
6-OH				8.10		
8-OH	11.63			11.95		

[a] Assignment by ^{1}H NMR experiments performed at 500 MHz.
[b] Assignment by ^{13}C NMR experiments performed at 125 MHz.
[c] The coupling constants cannot be assigned due to signal overlap.

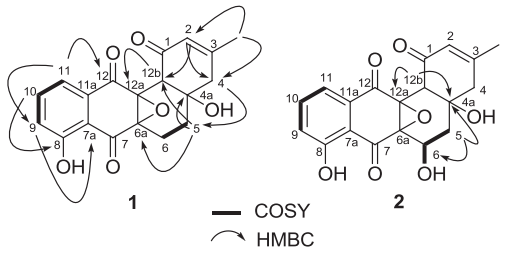

Figure 2. Key COSY and HMBC correlations of compounds **1** and **2**.

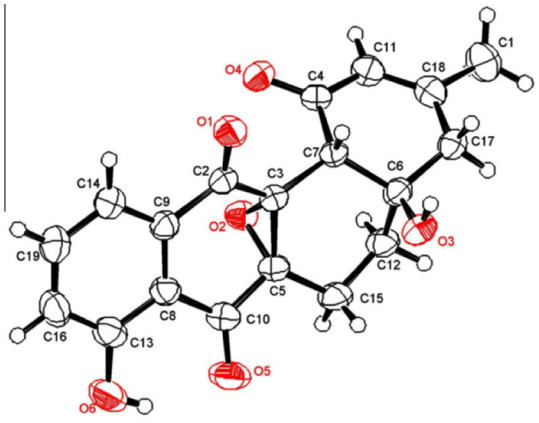

Figure 3. X-ray Oak Ridge Thermal Ellipsoid Plot (ORTEP) drawing of compound **1**.

between **1** and grecocycline A aglycon is the absolute configurations of the stereocenters at C-12b and C-4a. A hydroxyl group at C-6, similar to the one in angumycinone B (**2**), can also be observed in simocyclinone D4 aglycon, which contains additional hydroxyl groups at C-12b and C-7. However, the absolute configuration of

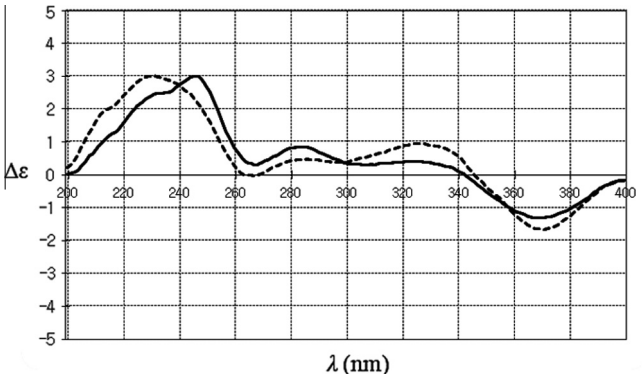

Figure 4. CD spectra of compounds **1** (---) and **2** (—).

these molecules has never been reported. Therefore, this Letter is the first report establishing the absolute configurations of angucyclic quinone structures via single-crystal X-ray diffraction analyses.

Compounds **1**–**8** were tested for their antimicrobial activity against four Gram-positive bacteria, including *Micrococcus luteus* KCCM1548, *Enterococcus hirae* KCCM11768, *Bacillus subtilis* KCTC1021, and *Staphylococcus aureus* CCARM3089 (MRSA), in addition to three Gram-negative bacteria (*Salmonella typhimurium* KCCM11862, *Klebsiella pneumonia* KCCM35454, and *Escherichia coli* KCTC2593) and three fungal strains (*Aspergillus fumigatus* HIC6094, *Trichophyton rubrum* KCCM60443, and *Candida albicans* KCCM11282) using previously described minimum inhibitory concentration (MIC) assay method.[30] Ampicillin and amphotericin B were used as positive controls for pathogenic bacteria and fungi, respectively. Ampicillin exhibited antimicrobial activities against *M. luteus*, *E. hirae*, *B. subtilis*, MRSA, *S. typhimurium*, *K. pneumonia*, and *E. coli* with MIC values of 0.78, 0.78, 3.13, 12.5, 12.5, 12.5, and 6.25 μg/mL, respectively. The MIC values of amphotericin B were 1.56 μg/mL against each fungal strain (*A. fumigatus*, *T. rubrum*,

and *C. albicans*). Angumycinone A (**1**) exhibited moderate antimicrobial activities against *M. luteus* and *E. hirae* (MIC values of 6.25 and 12.5 μg/mL, respectively); however, angumycinone B (**2**) was more active than **1** against the same strains (0.78 and 1.56 μg/mL, respectively). In addition, **2** demonstrated moderate activity against methicillin-resistant *S. aureus* (MRSA), displaying a MIC value of 12.5 μg/mL. The three known angucyclinone analogues, **3**, **5**, and **8**, also exhibited antimicrobial activity against *M. luteus* and *E. hirae*, while the other compounds (**4**, **6**, and **7**) were not active against any of the tested strains. MIC values of both compounds **3** and **5** were 0.39 and 0.78 μg/mL against *M. luteus* and *E. hirae*, respectively, while **8** displayed 0.39 μg/mL MIC value against both pathogenic bacteria. None of the compounds demonstrated any antimicrobial activity against the Gram-negative bacterial or fungal strains.

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Supplementary data

Supplementary data (experimental methods, X-ray data, NMR, HRFABMS and IR spectra of new compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.10.112.

References and notes

1. Bérdy, J. *J. Antibiot.* **2005**, *58*, 1–26.
2. Lam, K. S. *Curr. Opin. Microbiol.* **2006**, *9*, 245–251.
3. (a) Dharmaraj, S. World. *J. Microbiol. Biotechnol.* **2010**, *26*, 2123–2139; (b) Bull, A. T.; Stach, J. E. M. *Trends Microbiol.* **2007**, *15*, 491–499; (c) Fenical, W.; Jensen, P. R. *Nat. Chem. Biol.* **2006**, *2*, 666–673.
4. (a) Currie, C. R.; Scott, J. A.; Summerbell, R. C.; Malloch, D. *Nature* **1999**, *398*, 701–704; (b) Crawford, J. M.; Clardy, J. *Chem. Commun.* **2011**, 7559–7566.
5. (a) Takagi, M.; Shin-ya, K. *J. Antibiot.* **2012**, *65*, 443–447; (b) Olano, C.; Méndez, C.; Salas, J. A. *Mar. Drugs* **2009**, *7*, 210–248; (c) Oh, D.-C.; Scott, J. J.; Currie, C. R.; Clardy, J. *Org. Lett.* **2009**, *11*, 633–636; (d) Header, S.; Wirth, R.; Herz, H.; Spiteller, D. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 4742–4746; (e) Kroiss, J.; Kaltenpoth, M.; Schneider, B.; Schwinger, M.-G.; Hertweck, C.; Maddula, R. K.; Strohm, E.; Svatoš, A. *Nat. Chem. Biol.* **2010**, *6*, 261–263.
6. Johnson, D. B.; Hallberg, K. B. *Sci. Total Environ.* **2005**, *338*, 3–14.
7. (a) Johnson, D. B. *FEMS Microbiol. Ecol.* **1998**, *27*, 307–317; (b) Xie, J.; He, Z.; Liu, X.; Van Nostrand, J. D.; Deng, Y.; Wu, L.; Zhou, J.; Qiu, G. *Appl. Environ. Microbiol.* **2011**, *77*, 991–999.
8. (a) Park, H. B.; Kwon, H. C.; Lee, C.-H.; Yang, H. O. *J. Nat. Prod.* **2009**, *72*, 248–252; (b) Park, H. B.; Kim, Y.-J.; Park, J.-S.; Yang, H. O.; Lee, K. R.; Kwon, H. C. *J. Nat. Prod.* **2011**, *74*, 2309–2312; (c) Park, H. B.; Kim, Y.-J.; Lee, J. K.; Lee, K. R.; Kwon, H. C. *Org. Lett.* **2012**, *14*, 5002–5005.
9. Paululat, T.; Kulik, A.; Hausmann, H.; Karagouni, A. D.; Zinecker, H.; Imhoff, J. F.; Fiedler, H.-P. *Eur. J. Org. Chem.* **2010**, 2344–2350.
10. Gilpin, M. L.; Balchin, J.; Box, S. J.; Tyler, J. W. *J. Antibiot.* **1989**, *42*, 627–628.
11. Oka, M.; Kamei, H.; Hamagishi, Y.; Tomita, K.; Miyaki, T.; Konishi, M.; Oki, T. *J. Antibiot.* **1990**, *43*, 967–976.
12. Kaliappan, K. P.; Ravikumar, V. *J. Org. Chem.* **2007**, *72*, 6116–6126.
13. Hayakawa, Y.; Ha, S.-C.; Kim, Y. J.; Furihata, K.; Seto, H. *J. Antibiot.* **1991**, *44*, 1179–1186.
14. Puder, C.; Zeeck, A. *J. Antibiot.* **2000**, *53*, 329–336.
15. Parker, K. A.; Ding, Q.-J. *Tetrahedron* **2000**, *56*, 10249–10254.
16. Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, *9*, 103–137.
17. Xie, Z.; Liu, B.; Wang, H.; Yang, S.; Zhang, H.; Wang, Y.; Ji, N.; Qin, S.; Laatsch, H. *Mar. Drugs* **2012**, *10*, 551–558.
18. Bruntner, C.; Binder, T.; Pathom-aree, W.; Goodfellow, M.; Bull, A. T.; Potterat, O.; Puder, C.; Hörer, S.; Schmid, A.; Bolek, W.; Wagner, K.; Mihm, G.; Fiedler, H.-P. *J. Antibiot.* **2005**, *58*, 346–349.
19. Omura, S.; Nakagawa, A.; Fukamachi, N.; Miura, S.; Takahashi, Y.; Komiyama, K.; Kobayashi, B. *J. Antibiot.* **1988**, *41*, 812–813.
20. (a) Palmu, K.; Ishida, K.; Mäntsälä, P.; Hertweck, C.; Metsä-Ketelä, M. *ChemBioChem* **2007**, *8*, 1577–1584; (b) Kallio, P.; Liu, Z.; Mäntsälä, P.; Niemi, J.; Metsä-Ketelä, M. *Chem. Biol.* **2008**, *15*, 157–166.
21. *Angumycinone A (**1**):* colorless block crystal; mp 180–182 °C; $[\alpha]_D^{25}$ +112.0 (*c* 0.10, CH_3CN); CD (CH_3CN) λ_{max} ($\Delta\varepsilon$) 370 (−1.66), 325 (+0.96), 284 (+0.47), 231 (+3.03) nm; UV (CH_3CN) λ_{max} ($\log\varepsilon$) 360 (3.43), 236 (4.17), 204 (4.05) nm; IR (film) ν_{max} 3427, 1640, 1452, 1276, 969 cm^{-1}; ^1H and ^{13}C NMR spectra, see Table 1; HRFABMS $[M+H]^+$ *m*/*z* 341.1025 (calcd for $C_{19}H_{17}O_6$, 341.1025).
22. Taniguchi, M.; Nagai, K.; Watanabe, M.; Niimura, N.; Suzuki, K.; Tanaka, A. *J. Antibiot.* **2002**, *55*, 30–35.
23. Sasaki, T.; Gomi, S.; Sezaki, M.; Takeuchi, Y.; Kodama, Y.; Kawamura, K. *J. Antibiot.* **1988**, *41*, 843–848.
24. Fotso, S.; Mahmud, T.; Zabriskie, T. M.; Santosa, D. A.; Sulastri; Proteau, P. J. *J. Nat. Prod.* **2008**, *71*, 61–65.
25. Balci, M. Basic ^1H and ^{13}C NMR spectroscopy; Elsevier: Amsterdam, 2005; pp 130–132.
26. Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *39*, 876–881.
27. *Angumycinone B (**2**):* pale yellowish oil; $[\alpha]_D^{25}$ +115.2 (*c* 0.10, CH_3CN); CD (CH_3CN) λ_{max} ($\Delta\varepsilon$) 370 (−1.31), 325 (+0.41), 283 (+0.84), 246 (+3.00) nm; UV (CH_3CN) λ_{max} ($\log\varepsilon$) 361 (3.45), 236 (4.19), 204 (4.04) nm; IR (film) ν_{max} 3417, 1651, 1455, 1267, 1088 cm^{-1}; ^1H and ^{13}C NMR spectra, see Table 1 ; HRFABMS $[M+H]^+$ *m*/*z* 357.0980 (calcd for $C_{19}H_{17}O_7$, 357.0974).
28. Holzenkämpfer, M.; Walker, M.; Zeeck, A. *J. Antibiot.* **2002**, *55*, 301–307.
29. (a) Sun, C.-H.; Wang, Y.; Wang, Z.; Zhou, J.-Q.; Jin, W.-Z.; You, X.-F.; Gao, H.; Zhao, L.-X.; Si, S.-Y.; Li, X. *J. Antibiot.* **2007**, *60*, 211–215; (b) Tsukuda, E.; Tanaka, T.; Ochiai, K.; Kondo, H.; Yoshida, M.; Agatsuma, T.; Saitoh, Y.; Teshiba, S.; Matsuda, Y. *J. Antibiot.* **1996**, *49*, 333–339.
30. Park, H. B.; Yang, H. O.; Lee, K. R.; Kwon, H. C. *Molecules* **2011**, *16*, 3519–3529.