Angucyclinones from an Indonesian *Streptomyces* sp.

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Six new angucyclinone polyketides named panglimycins A−F were isolated together with the three known metabolites (+)-fujianmycin A, (+)-ochromycinone, and emycin C from the bioassay-guided fractionation of the extract of the Indonesian *Streptomyces* strain ICBB8230. The new compounds are highly oxygenated angucyclinones that appear to be biosynthetically derived from ochromycinone or fujianmycin. Their structures were determined by X-ray crystal analysis, interpretation of 1D- and 2D-NMR spectra, and comparison of the data with those of structurally related known natural products. Despite structural similarities to angucyclinones with antibiotic activities, the panglimycins did not exhibit any growth inhibition when tested against several bacteria and fungi.

We recently began a screening program to discover new antibiotics from microorganisms isolated from the Black Water Ecosystem in Kalimantan, Indonesia. During our initial survey of *Streptomyces* spp., the antibiotic activity of the crude extract of the isolate ICBB8230 against *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Candida albicans* drew our attention. Chromatographic separation of the extract and analysis using an antibacterial agar diffusion assay led to the known angucyclinone antibiotics (+)-fujianmycin A[1] and (+)-ochromycinone.[2,3] During the processing of the extract to find the antibiotic compounds, it was noticed that the organism also produced additional angucyclinone metabolites. This family of antibiotics is characterized by a tetracyclic framework assembled in an angular manner, leading to the benz[*a*]anthracene system. These polyketide natural products have attracted much attention due to their biological activity, interesting chemical structures, and biosynthesis.[4] Further workup of the extract led to the isolation of the new angucyclinones panglimycins A (**1a**), B (**1b**), C (**1c**), D (**2a**), E (**2b**), and F (**3**) and the known compound emycin C.[5] The name panglimycin signifies the isolation of the producing strain from soil of the Black Water River, Pangkoh Lima. The known compounds were identified by substructure searches in AntiBase.[6] Here we report the isolation, structure elucidation, and biological activity testing of the new compounds.

Results and Discussion

A culture of the strain ICBB8230, identified as a *Streptomyces* sp., in M_2 medium delivered a greenish culture broth, which was processed as indicated in the experimental section. Two crude extracts were obtained, one from the mycelium and one from the culture broth. They were fractionated using various chromatographic techniques.

Compound **1a** was isolated as colorless crystals. An AntiBase search provided elmycin A (**4**) as a likely possibility, but the ^{1}H NMR shifts differed slightly from those published.[7] The ^{13}C NMR shifts for **4** were reported in $CDCl_3$, but **1a** was not soluble in $CDCl_3$, so a ^{13}C NMR spectrum was obtained in DMSO-d_6. The necessity to use a different NMR solvent, as well as shift differences, suggested that **1a** was not identical to **4**. In order to further assess the structure of **1a**, an X-ray crystal structure was obtained. The relative configuration of **1a** is shown in Figure 1 and differs from that of **4**[8] at C-6a and C-12a, indicating that **1a** is a stereoisomer of elmycin A, which we have named panglimycin A. Although the absolute configuration was not determined experimentally, we propose the 3*S*,6*R*,6a*S*,7*S*,12a*S* configuration based on the likely derivation of compound **1a** from (+)-ochromycinone (3*S* configuration),[9] which was also isolated from the ICBB8230 strain.

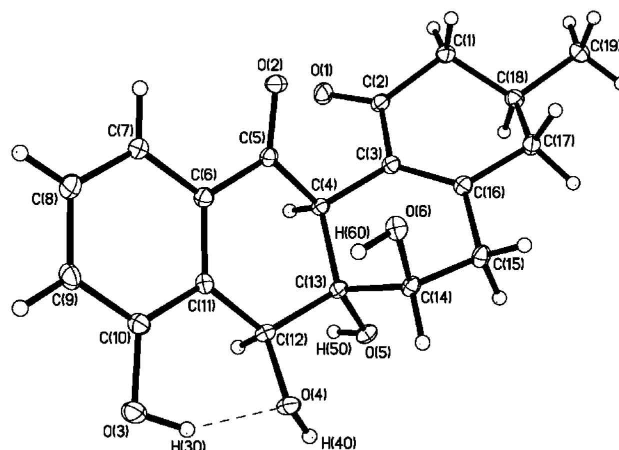

Figure 1. ORTEP representation of panglimycin A (**1a**).

Compound **1b** was obtained as a yellowish powder. Extensive NMR (^{1}H, ^{13}C, DEPT, COSY, HSQC, HMBC) and MS data were used to establish the structure. The ^{1}H−^{1}H-COSY spectrum indicated three coupled spin systems, along with two methines at δ 5.50 and 3.90 that appeared as singlets. The first spin system involved two doublets of doublets at δ 7.31 and 7.00 ($J = 7.8$, 1.1 Hz) and an apparent triplet at δ 7.20 ($J = 7.8$ Hz), which can be attributed to a 1,2,3-trisubstituted aromatic system. The second spin system consists of a methylene (δ 3.08, 2.26) adjacent to a methine (δ 4.47) attached to an oxygenated carbon. The final spin system has a methylene (δ 2.56) coupled to a methine at δ 2.18 bearing a methyl group (δ 1.23) and also attached to another methine (δ 4.11) on a carbon bearing an oxygen. The ^{13}C NMR spectrum indicated 19 carbon resonances as required by the high-resolution mass. There were two carbonyls at δ 200.5 and 196.3, three sp^2 methines, five sp^3 methines including three bearing oxygen, one methyl, two methylene carbons, and five sp^2 and one sp^3 quaternary carbons. The (+)-ESIMS indicated the pseudomolecular ion at m/z 361 [M + H]$^+$, and the HRESIMS delivered the molecular formula

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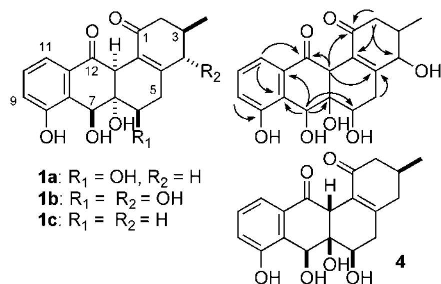

Figure 2. Panglimycins A–C (**1a–c**), selected HMBC correlations in panglimycin B, and the structure of elmycin A (**4**).

Table 1. ^{13}C NMR (75 MHz) Data for Compounds **1a–c**, **2a**, **2b**, and **3** in MeOH-d_4

position	δ_C					
	1a[a]	**1b**	**1c**	**2a**	**2b**	**3**
1	197.3	200.5	201.5	198.9	200.1	208.6
2	45.4	45.4	46.8	44.8	46.3	49.3
3	30.0	40.5	31.8	40.7	31.7	30.7
3-Me	21.2	19.1	21.7	18.5	21.6	22.1
4	39.0	76.6	40.2	74.7	39.0	41.7
4a	153.3	159.4	159.5	153.7	153.4	77.1
5	38.1	35.4	29.2	48.4	51.7	28.7
6	64.3	66.2	23.7	57.1	57.2	24.6
6a	76.0	77.7	77.6	75.8	75.9	69.0
7	74.9	76.8	75.1	75.6	75.8	64.8
7a	126.9	128.1	126.8	125.0	125.0	128.1
8	155.9	157.6	158.9	158.7	158.8	157.2
9	119.9	121.8	123.4	123.2	123.1	122.1
10	127.8	129.5	130.3	130.2	130.2	130.9
11	115.9	118.1	119.6	119.6	119.6	119.3
11a	133.9	135.3	133.0	133.1	133.3	132.1
12	193.2	196.3	197.4	195.5	195.7	194.9
12a	49.7	51.0	52.6	50.7	50.7	67.3
12b	127.1	129.4	129.1	132.7	131.7	77.3

[a] DMSO-d_6.

$C_{19}H_{20}O_7$. The general NMR characteristics indicated that **1b** was quite similar in structure to **1a**.

In the HMBC spectrum, H-9 (δ 7.00) and H-10 (δ 7.20) showed cross-peaks to C-8 (δ 157.6), suggesting an oxygenated carbon in the aromatic ring (Figure 2). The proton at δ 7.31 (H-11) correlated to the carbonyl at δ 196.3, suggesting a carbonyl adjacent to the trisubstituted aromatic system. The singlet at δ 5.50 (H-7) had correlations to the carbons at δ 157.6 (C-8), 128.1 (C-7a), and 77.7 (C-6a), establishing a secondary alcohol at C-7. Further correlations were seen between the three methines H-7 (δ 5.50), H-6 (δ 4.47), and H-12a (δ 3.90) to the quaternary sp^3 carbon at δ 77.7 and also between both methine H-7 and H-12a to the carbon C-6 (δ 66.2). On the other hand, the methine at δ 3.90 and the methylene H$_2$-2 (δ 2.56) showed correlations to carbons at δ 200.5 (C-1) and 129.4 (C-12b), while the methyl doublet correlated to the methylene carbon C-2 (δ 45.4) and both methine carbons at δ 76.6 (C-4) and C-3 (δ 40.5), confirming the third spin system from the ^{1}H–^{1}H-COSY. On the basis of these correlations and comparison with **1a**, the structure of **1b** was determined and named panglimycin B. Panglimycin B (**1b**) is a 4-hydroxy analogue of **1a**. As shown in Table 1, the key differences in ^{13}C NMR shifts between **1a** and **1b** are at C-4 and nearby carbons.

The similarities in chemical shifts to **1a** suggest that the same relative configuration at the ring junction (C-6a/C-12a) is shared by **1b**. The *trans* relative configuration at C-3 and C-4 of **1b** is proposed on the basis of the NOESY spectrum, which revealed an important correlation between the H-4 and CH$_3$-3 protons (Figure 3), and on the large coupling constant between H-3 and H-4 ($J_{H\text{-}3/H\text{-}4} = 9.0$ Hz), which represents a diaxial-like relationship for these protons.[1] This is the same relative configuration seen in (+)-fujianmycin A,[1] which is also present in this extract and is a possible biosynthetic precursor to **1b**. The presence of a strong NOESY correlation between H-7 and H-12a is also supportive of the proposed ring junction configuration. These observations led to the proposed relative configuration of **1b** as shown in Figure 2. An attempt to determine the absolute configuration of **1b** was done using the Mosher method, but the derivatization reaction led only to a complex mixture of decomposition products.

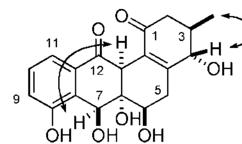

Figure 3. Observed NOESY correlations in panglimycin B (**1b**) and proposed relative configuration.

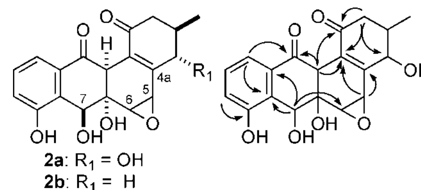

Figure 4. Structures of panglimycins D (**2a**) and E (**2b**) and key HMBC correlations for panglimycin D.

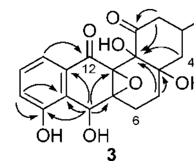

Figure 5. Selected HMBC correlations in panglimycin F (**3**).

Compound **1c** appeared as a yellow oil, and it exhibited similar ^{1}H and ^{13}C NMR spectra to **1b**, with the same 1,2,3-trisubstituted aromatic region, the methines at δ 5.42 and 3.90, and the methyl doublet at δ 1.13. The major differences in the ^{1}H NMR spectrum for **1c** were the absence of the protons at δ 4.47 (H-6) and 4.11 (H-4) and a more complex region in the range of δ 2.58–2.00. The molecular formula was deduced from the (+)-HRESIMS to be $C_{19}H_{20}O_5$, which requires 10 unsaturations as in **1b**, but two fewer oxygen atoms are present in **1c**. The ^{13}C NMR spectrum of **1c** lacks the carbon resonances that appear in **1b** at δ 76.6 (C-4) and 66.2 (C-6) and instead has two methylene carbon signals at δ 40.2 and 23.7. Extensive interpretation of the HMBC spectrum correlations, combined with comparison of data with those of **1b**, established that **1c** was missing the oxygens from C-4 and C-6. The resulting compound **1c** was named panglimycin C.

Compound **2a** was obtained as a yellowish powder like **1b**. The proton NMR spectrum of **2a** is also similar to those of **1a**, **1b**, and **1c** with the trisubstituted aromatic system and the methyl doublet in the aliphatic region. The main difference between the **2a** and **1b** spectra is that the H-5/H-6 spin system has been replaced by two coupled protons at δ 3.97 and 3.94. The molecular weight was deduced from the (+)-ESIMS to be 358. The HRESIMS gave the molecular formula $C_{19}H_{18}O_7$, requiring 11 unsaturations instead of 10 as in **1b** and **1c**, suggesting the presence of an additional double bond or ring. The presence of two new sp^3 methine carbon signals at δ 57.1 and 48.4 and the lack of additional sp^2 carbon signals compared to **1b** suggested the presence of an epoxide in view of the chemical shifts of the methine carbons. The location of the epoxide was deduced from the HMBC spectrum, which indicated important correlations of the methine proton at δ 5.56 (H-7) to the carbon at δ 57.1 and of the methine proton at δ 4.35 (H-4) to the carbon at δ 48.4. These correlations indicated that the epoxide lies between C-4 and C-7, securing the structure of compound **2a**, which was named panglimycin D.

Table 2. ^{1}H NMR (300 MHz) Data for Panglimycins A−C (**1a**−**c**)

	δ_H (*J* in Hz)		
position	**1a**[a]	**1b**[b]	**1c**[b]
2	2.10–2.40, m	2.56, m	2.15–2.58, m
3	2.10–2.40, m	2.18, m	2.15–2.58, m
3-Me	1.07, d (5.7)	1.23, d (6.5)	1.13, d(5.9)
4	2.10–2.40, m	4.11, d (9.0)	2.15–2.58, m
5	2.59, dd (19.7, 4.2) 2.00, d (19.7)	3.08, dd (20.2, 4.6) 2.26, d (20.2)	2.12, m 1.38, m
6	4.16, br t (3.2)	4.47, br d (3.9)	2.15–2.58, m
7	5.38, s	5.50, s	5.42, s
9	6.96, dd (7.2, 2.0)	7.00, dd (7.8, 1.1)	7.05, dd (7.7, 1.3)
10	7.14, m	7.20, dd (7.8, 7.8)	7.25, ddd (7.7, 7.7, 0.8)
11	7.14, m	7.31, dd (7.8, 1.1)	7.39, dd (7.7, 1.3)
12a	3.74, s	3.90, s	3.90, br d (1.9)

[a] DMSO-d_6 additional signals at δ 5.14 (C-6-O*H*), δ 4.68 (C-7-O*H*). [b] MeOH-d_4.

Table 3. ^{1}H NMR (300 MHz) Data for Panglimycins D−F (**2a**, **2b**, and **3**) in MeOH-d_4

	δ_H (*J* in Hz)		
position	**2a**	**2b**	**3**
2	2.53, m	2.30–2.57, m	2.60, dd (8.6, 2.5) 2.22, m
3	2.19, m	2.30–2.57, m	2.22, m
3-Me	1.25, d (6.5)	1.18, d (6.1)	1.03, d (6.0)
4	4.35, d (8.5)	2.71, dd (18.4, 4.0) 2.30–2.57, m	1.97, m 1.61, ddd (14.1, 2.6, 2.6)
5	3.97, dd (4.3, 1.5)	3.92, dd (4.1, 1.4)	1.97, m 1.36, m
6	3.94, d (4.3)	3.42, d (4.1)	2.90, ddd (16.3, 15.2, 6.0) 2.22, m
7	5.56, s	5.56, s	5.39, s
9	7.05, dd (8.1, 1.3)	7.05, dd (7.2, 1.2)	7.30, m
10	7.26, ddd (8.1, 7.8, 0.8)	7.26, dd (7.9, 7.9)	7.30, m
11	7.39, dd (7.8, 1.3)	7.42, dd (7.9, 1.2)	7.13, m
12a	3.99, d (1.3)	4.00, s	

Due to the close proximity of the chemical shifts for the epoxide protons and H-12a in MeOH-d_4, a NOESY spectrum was recorded in acetone-d_6 to aid in determining the relative configuration of compound **2a**. The NOESY spectrum exhibited cross-peaks between H-7 and H-12a and between H-4 and the C-3 methyl protons, which is consistent with the relative configuration observed for panglimycin B (**1b**), but no correlations were seen to the epoxide protons. Furthermore, preliminary molecular modeling of **2a** (Chem3D) suggested that a H-5 to H-4 correlation, if observed, could be possible for both configurations of the epoxide. Therefore, the relative configuration of the epoxide remains unassigned. The coupling constant of 8.5 Hz from H-3 to H-4 also supports the *trans* relative configuration at C-3/C-4.[1]

Compound **2b** was also obtained as a yellowish oil. Compound **2b** was found to have MS and NMR data similar to elmycin B, but as seen with **1a**, the NMR shifts were not an exact match.[7] Further, the optical rotation of **2b** was −31°, while the literature value for elmycin B was +28.5°. A comparison of the ^{13}C NMR shifts for **2b** and **2a** illustrates that the only major differences between the two lie near C-4, the site of the hydroxyl in **2a**. This suggests that **2b** is in the same stereochemical series as is **2a** and that it is a stereoisomer of elmycin B, which we have named panglimycin E (**2b**).

Compound **3** was obtained as a colorless oil. The molecular formula $C_{19}H_{20}O_7$ obtained from HRESIMS requires 11 unsaturations as in **2a**. The ^{1}H−^{1}H-COSY spectrum indicated the presence of the trisubstituted aromatic system and two additional fragments; one consisted of CH_2CH_2 and the second fragment included a methyl doublet at δ 1.03, a methine at δ 3.97, and two methylene groups (δ 2.60, 2.22; δ 1.97, 1.61) that were assembled in the same manner as H-2 to H-4 in **1a**, **1c**, and **2b**. The shifts of the H-4 protons, however, were upfield relative to the H-4 protons in **1a**, **1c**, and **2b**, suggesting a change in the hybridization at C-4a. The ^{13}C NMR spectrum of **3** indicated 19 carbon resonances, comprised of two carbonyls at δ 208.6 and 194.9, three sp^2 methines, three sp^2 quaternary carbons, two sp^3 methines, four methylenes, one methyl, and four quaternary sp^3 carbons. The downfield shift of the C-1 carbonyl, the reduction in the number of sp^2 quaternary carbons, and the addition of new carbon resonances between 70 and 80 ppm suggested the possible dihydroxylation of the isolated double bond between C-4a and C-12b. The lack of a C-4a/C-12b double bond would require an additional ring in **3**.

The HMBC spectrum revealed correlations between H-2, H-4, and H-5 and the carbons at δ 77.3/77.1, which correspond to C-12b and C-4a, confirming the oxygenation of the C-4a/C-12b double bond. The H-7 proton correlates to the methylene carbon at δ 24.6, the quaternary carbons at δ 67.3 and 69.0, and the carbon at δ 77.3, suggesting that C-6a and C-12a also bear oxygen groups. Furthermore the correlation of H-5 and H-6 to the quaternary carbon at δ 69.0 defines this carbon as C-6a. On the basis of the need for an additional ring in **3** and the presence of epoxides in a number of known angucyclinones, a reasonable conclusion is that an epoxide lies somewhere on the C-4a/C-12b/C-12a/C-6a backbone. The chemical shifts of these four carbons (77.1, 77.3, 67.3, and 69.0, respectively) and comparisons with NMR data for the related compounds simocyclinone D8[10] and elmycin C[11] suggest that the epoxide is formed between C-6a and C-12a, but further confirmation was necessary. When the ^{1}H NMR spectrum was recorded in DMSO-d_6, all four exchangeable protons present in **3** were observed. The phenolic hydroxy proton appeared at 10 ppm and the C-7 hydroxy proton was revealed by coupling with H-7, which left two hydroxy proton resonances (4.53 and 4.39 ppm) to be assigned. The HMBC spectrum of **3** in DMSO-d_6 provided the necessary correlations. The 4.53 ppm proton was correlated with carbons C-12a, C-12b/C-4a, and C-1, while the 4.39 ppm proton correlated to carbons at C-12b/C-4a and C-4. These correlations place the hydroxy groups at C-4a and C-12b, and therefore, the epoxide spans C-6a to C-12a, securing the structure of panglimycin F (**3**). The structure of panglimycin F is very similar to that of elmycin C[11] and simocyclinone A_1,[12] the only differences in the planar structures being the presence of an additional C5−C6 double bond in elmycin C and a C2−C3 double bond in simocyclinone A_1.

Biological Activities. Panglimycins A−E are related to the known antibiotics elmycins A (**4**) and B, which exhibited antibacte-

rial and antifungal activities, as well as potent action against protozoa, especially *Trichomonas vaginalis*.[7] In contrast, the panglimycins did not show antibiotic activity. Compounds **1a**−**c**, **2a**,**b**, and **3** were tested against the bacteria *Staphylococcus aureus, Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, the fungus *Mucor miehei*, and the yeast *Candida albicans* in the agar diffusion test, at concentrations ranging from 20 to 120 μg/disk, but no growth inhibition was observed. In contrast, both ochromycinone (17 μg/disk) and fujianmicin A (18 μg/disk), as positive controls, showed clear zones of inhibition against *B. subtilis* and *P. aeruginosa*. This difference in biological activity may be attributed to the opposite configuration at the C-6a/C-12a ring junction compared to elmycin A, which results in significantly different overall molecular shapes for the panglimycins.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Jasco P1010 polarimeter. NMR spectra were measured on a Bruker Unity 300 MHz spectrometer. The spectra were referenced to the solvent line methyl at 3.30 ppm for ^{1}H NMR spectra and to the center line of the MeOH-d_4 septet at 49.15 ppm for ^{13}C NMR spectra. ESIMS data were recorded on a ThermoFinnigan LCQ Advantage system. HRESI mass spectra were recorded on a Waters/Micromass LCT spectrometer. HREIMS and HRCIMS were measured on a JEOL HMS-600H MS route magnetic sector instrument. IR spectra were recorded on a Nicolet Nexus 470 FT-IR spectrometer. UV–vis spectra were recorded on a Beckmann DU 640 B spectrophotometer. Preparative HPLC was performed using an RP18 column (Phenomenex, RP 100-C18, 5 μm) with the detector set at 254 nm. Flash chromatography was carried out on Si gel (230–400 mesh). Thin-layer chromatography was performed on aluminum sheets with Si gel 60 F_{254} (EMD chemicals Inc.). Size exclusion chromatography was done on Sephadex LH-20 (Pharmacia). M_2 medium: 4 g of glucose, 4 g of yeast extract, and 10 g of malt extract were dissolved in 1000 mL of deionized H_2O, the pH was adjusted to 7.8 with 2 N NaOH, and the medium was sterilized at 121 °C for 35 min.

Organism Collection and Identification. Samples were taken from soil of the Black Water River, Pangkoh Lima, Malibu Village, Gandang Subdistrict, Pulang Pisau Regency, Central Kalimantan Province, Indonesia. This river is part of the unique Black Water ecosystem in Kalimantan. The ecosystem lies in the remote area about 150 km from the coast of South Kalimantan. Soil samples were stored at room temperature.

The selective agar plate medium was obtained by the addition of antifungal antibiotics and bacterial inhibitors (20 mg/L trimethoprim, 50 mg/L griseofulvin, 50 mg/L nystatin) into the YM medium (4 g/L glucose, 10 g/L malt extract, 4 g/L yeast extract) adjusted to pH 7. The antibiotics were dissolved in sterile water and added to the autoclaved agar medium prior to the pouring of the plates. Five grams of soil was inoculated into a 15 mL test tube containing 9 mL of sterilized H_2O containing 0.85% NaCl, followed by serial dilutions. The soil suspension from the 10^{-3} dilution (0.1 mL) was spread on selective agar plates. The plates were incubated at 30 °C until the colonies appeared (4–7 days). The colonies with different characteristics were transferred repeatedly to selective agar plates until pure cultures were obtained. Each colony was checked by microscopy to differentiate between actinomycetes and other microorganisms. The *Streptomyces* sp. ICBB8230 culture was deposited at ICBB-CC (Indonesian Center for Biodiversity and Biotechnology Culture Collection of Microorganisms) as 0.5 mL of a 20% glycerol stock stored at −20 °C.

The 16S rRNA gene sequence of *Streptomyces* sp. ICBB8230 was found to be identical over the sequenced region to that of *Streptomyces* sp. CNR875 PL04, isolated from marine sediment collected near Palau (see Supporting Information for details).

Fermentation and Isolation. *Streptomyces* sp. ICBB8230 was cultivated on a 5 L scale using 1 L Erlenmeyer flasks containing 250 mL of M_2 medium at 28 °C for 4 days on a rotary shaker (300 rpm). The greenish culture broth was mixed with ca. 2.0 kg of Celite and filtered under vacuum. The filtered medium was passed through a HP-20 Diaion column (3 × 17 cm), and the resin was washed with distilled H_2O and eluted with MeOH. The mycelium was extracted sequentially with EtOAc and then MeOH. Both extracts were evaporated to dryness separately. The combined mycelium extract (500 mg) was chromatographed on Sephadex LH-20 (50% MeOH/CH_2Cl_2), resulting in six fractions, I−VI. Fraction IV exhibited the main biological activity against *E. coli*, *Ps. aeruginosa*, and *C. albicans*. Fraction IV was chromatographed on Sephadex LH-20 (MeOH) and delivered four subfractions, IVA−IVD. Preparative TLC (PTLC; 5% MeOH/CH_2Cl_2) of the active subfractions IVB and IVC gave ochromycinone (30 mg), fujianmycin A (50 mg), and emycin C (1.5 mg). The crude extract from the medium (2 g) was first separated on Sephadex LH-20 (MeOH), yielding six fractions, I−VI. Fractions I and II contained only fatty acids and were discarded. Fraction IV was first separated on preparative HPLC using a gradient from 20% to 100% MeOH in H_2O and delivered panglimycins A (**1a**, 5 mg) and E (**2b**, 4 mg) and a mixture of two compounds. The mixture was further purified by PTLC (8% MeOH/CH_2Cl_2) and led to panglimycins C (**1c**, 2.5 mg) and F (**3**, 3 mg). The purification of fraction V twice over Sephadex LH-20 (MeOH) delivered two subfractions, VA and VB. The subfraction VA was washed with CH_2Cl_2 and gave a mixture of ochromycinone and fujianmycin A and a CH_2Cl_2-insoluble yellowish powder, panglimycin B (**1b**, 102 mg). The subfraction VB was purified by PTLC and gave panglimycin B (**1b**, 7 mg) and panglimycin D (**2a**, 110 mg).

Panglimycin A (1a): colorless crystals (50% MeOH/CH_2Cl_2); $[\alpha]^{23}_D$ +83 (*c* 0.06, MeOH); UV (MeOH) λ_{max} (log ϵ) 311 (2.92), 247 (3.59), 209 (3.82) nm; IR (neat) ν_{max} 3299, 2915, 2847, 1695, 1652, 1634, 1587, 1559, 1463, 1293, 1055, 1003, 938, 839, 793 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; (+)-HRESIMS *m/z* 345.1327 (calcd for $C_{19}H_{21}O_6$, 345.1338) and 367.1165 (calcd for $C_{19}H_{20}O_6Na$, 367.1358).

Panglimycin B (1b): light yellow solid; $[\alpha]^{27}_D$ −100 (*c* 0.06, MeOH); UV (MeOH) λ_{max} (log ϵ) 321 (2.92), 262 (3.50), 222 (4.18) nm; IR (neat) ν_{max} 3347, 2958, 2922, 2854, 1657, 1588, 1464, 1390, 1297, 1263, 1085, 1062, 1023, 996, 939, 796, 737 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; (+)-ESIMS *m/z* 361 ([M + H]$^+$, 26), 743 ([2M + Na]$^+$, 100); (+)-HRESIMS *m/z* 361.1283 (calcd for $C_{19}H_{21}O_7$, 361.1287).

Panglimycin C (1c): yellow oil; $[\alpha]^{27}_D$ −28 (*c* 0.04, MeOH); UV (MeOH) λ_{max} (log ϵ) 328 (3.20), 263 (sh), 243 (4.14) nm; IR (neat) ν_{max} 3330, 2955, 2926, 1670, 1653, 1583, 1458, 1393, 1282, 1077, 797, 1385, 1107 cm^{-1}; NMR data, see Tables 1 and 2; (+)-ESIMS *m/z* (%) 329 ([M + H]$^+$, 95), 679 ([2M + Na]$^+$, 100); HREIMS *m/z* 328.1298 (calcd for $C_{19}H_{20}O_5$, 328.1311).

Panglimycin D (2a): light yellow solid; $[\alpha]^{27}_D$ −30 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 324 (2.90), 261 (3.80), 242 (3.77) nm; IR (neat) ν_{max} 3212, 2955, 1685, 1656, 1634, 1580, 1463, 1291, 1271, 1234, 1152, 1083, 892, 786 cm^{-1}; NMR data, see Tables 1 and 3; (+)-ESIMS *m/z* (%) 381 ([M + Na]$^+$, 18), 739 ([2M + Na]$^+$, 100); (+)-HRESIMS *m/z* 381.0978 (calcd for $C_{19}H_{18}O_7Na$, 381.0950).

Panglimycin E (2b): yellowish oil; $[\alpha]^{23}_D$ −31 (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 315 (3.81), 254 (4.39), 228 (sh), 207 (4.45) nm; IR (neat) ν_{max} 3360, 2949, 1676, 1608, 1580, 1463, 1383, 1296, 1278, 1243, 1092, 1030, 900, 789 cm^{-1}; NMR data, see Tables 1 and 3; (+)-ESIMS *m/z* = 343 ([M + H]$^+$, 10), 365 ([M + Na]$^+$, 15), 707 ([2M + Na]$^+$, 100); (+)-HRESIMS 343.1157 (calcd for $C_{19}H_{19}O_6$, 343.1182) and 365.0988 (calcd for $C_{19}H_{18}O_6Na$, 365.1001).

Panglimycin F (3): colorless oil; $[\alpha]^{27}_D$ +150 (*c* 0.09, MeOH); UV (MeOH) λ_{max} (log ϵ) 332 (3.42), 272 (3.94), 247 (4.13) nm; IR (neat) ν_{max} 3360, 2956, 2917, 2849, 1698, 1662, 1640, 1456, 1266, 1221, 1157, 1089, 1071, 738 cm^{-1}; NMR data in MeOH-d_4, see Tables 1 and 3; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.10 (1H, br s, C-8 O*H*), 7.30 (1H, br dd, *J* = 8.1, 8.1 Hz, H-10), 7.18 (1H, d, *J* = 8.1 Hz, H-11), 7.16 (1H, d, *J* = 8.1 Hz, H-9), 5.78 (1H, d, *J* = 9.2 Hz, C-7 O*H*), 5.10 (1H, br s, H-7), 4.53 (1H, s, C-12a O*H*), 4.39 (1H, s, C-4a O*H*), 2.72 (1H, m, H-6a), 2.36 (2H, m, H-2), 2.15 (1H, br dd, *J* = 15.6, 4.8 Hz, H-6b), 2.15 (1H, m, H-4a), 2.00 (1H, m, H-3), 1.79 (1H, m, H-5a), 1.45 (1H, br d, *J* = 13.3 Hz, H-4b), 1.20 (1H, m, H-5b), 0.92 (3H, d, *J* = 6.0 Hz, C-3 CH_3); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 206.8 (C, C-1), 193.5 (C, C-12), 155.5 (C, C-8), 130.6 (C, C-11a), 129.3 (CH, C-10), 127.0 (C, C-7a), 120.9 (CH, C-9), 117.2 (CH, C-11), 75.5* (C, C-4a), 75.3* (C, C-12b), 67.4 (C, C-6a), 65.5 (C, C12-a), 62.8 (CH, C-7), 47.3 (CH_2, C-2), 40.4 (CH_2, C-4), 28.7 (CH, C-3), 27.2 (CH_2, C-6), 23.0 (CH_2, C-5), 21.2 (CH_3, C-3 CH_3) (*assignments interchangeable); (+)-ESIMS *m/z* (%) 383 ([M + Na]$^+$, 100), 743 ([2M + Na]$^+$, 55); (+)-HRESIMS *m/z* 383.1115 (calcd for $C_{19}H_{20}O_7Na$, 383.1107).

X-ray crystallographic analysis of compound 1a: $C_{19}H_{20}O_6$, M_r = 344.35, orthorhombic, space group $P2_12_12_1$ (no. 24), a = 7.5554(11) Å, b = 9.0441(13) Å, c = 22.351(3) Å, V = 1527.3(4) Å^3, Z

= 4, D_{calcd} = 1.498 g cm^{-3}, μ = 0.112 mm^{-1}, 10 222 reflections measured, 3529 reflections independent (R_{int} = 0.0146), R_w = 0.0294, R_w = 0.0794. X-ray diffraction experiments for panglimycin A were carried out on a Bruker Smart Apex CCD diffractometer at 173 K using Mo Kα radiation (λ = 0.71070 Å). Absorption corrections were done by SADABS.[13] The structure was solved using direct methods and refined with full-matrix least-squares methods based on F^2. Non-hydrogen atoms were refined with anisotropic thermal parameters. The H atoms were located by difference Fourier synthesis and refined with isotropic thermal parameters. The absolute structure of the compound has not been determined based on the X-ray diffraction data; the anomalous scattering power is too small. All calculations were performed using the SHELXTL (v. 6.10) package.[14] Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (deposit No. CCDC 666383). 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-(0)223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **1a**–**c**, **2a**, **2b**, and **3**, COSY, HSQC, and HMBC spectra for **1b** and **2a**, details of the 16S rDNA analysis, and a Crystallographic Information File (CIF) for **1a**. This material is available free of charge at http://pubs.acs.org.

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