

## **Supporting Information**

### **New Cytotoxic 14-Membered Macrolides from Marine-derived Fungus *Aspergillus ostianus***

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## Experimental Section

**General Experimental Procedures.** Optical rotation values were determined on a JASCO P-1010 polarimeter. IR spectra were measured with JASCO FT/IR-420. High-resolution MS spectra were obtained with a Waters LCT-Premier 2695 mass spectrometer. 1D and 2D NMR were recorded on Bruker ARX-400, JEOL JNM-AL 400, JEOL GSX-400, and Bruker Avance 700 spectrometers. Chemical shifts ( $\delta$ ) are expressed in parts per million (ppm) with reference to the solvent signals with resonances at  $\delta_{\text{C/H}}$  77.0/7.25 (CDCl<sub>3</sub>) and 128.0/7.20 (C<sub>6</sub>D<sub>6</sub>). Normal-phase flash column chromatography (NP-FCC) was carried out on silica gel (40-63  $\mu\text{m}$ , Merck Co.). Reversed-phase column chromatography (RP-FCC) was carried out with Cosmosil 75 C<sub>18</sub>-OPN. Thin layer chromatography was carried out on silica gel 60 F<sub>254</sub> plates (Merck Co.). Cultivation of the titled fungus was performed in a Sanyo Grows Cabinet NLR-350H. HPLC was done using a Tosoh CCPS. UV and RI detectors were Tosoh UV-8020 and Shodex RI-102, respectively.

**Fungal Isolation and Identification.** The fungus, *Aspergillus ostianus* designated as strain 01F313, was isolated from an unidentified marine sponge collected in Pohnpei in 2001. Isolation and identification of the strain are described in the literature.<sup>2</sup> The fungus is maintained on 1/10 YSA medium at the Marine Natural Products Laboratory, Faculty of Pharmaceutical Sciences, The University of Tokushima, Japan.

**Cultivation of Fungus and Isolation of Metabolites.** The fungus was cultured for five weeks at 20° C in sixty seven 500 mL Erlenmeyer flasks each containing 150 mL of a 1/2 PD medium [Potato (100

g) and *D*-glucose (10 g) were boiled with 1 L of an aqueous (distilled water) solution of NaBr (47.50 g), KBr (1.14 g), CaBr<sub>2</sub> (2.48 g), and MgSO<sub>4</sub> (5.94 g) (bromine-modified artificial seawater) for 10 min.] Acidity of the medium was adjusted to pH 8.3 with 1 *M* HBr and 1 *M* NaOH.]. The broth was filtered, and the filtrate was passed through a column packed with HP-20 (205 g). After washing with 1 L of distilled water, methanol (6 L) was passed through the column and the methanol solution was concentrated. The brown extract (2.04 g) was separated by NP-FCC (205 g of silica gel) eluted with CHCl<sub>3</sub>-MeOH gradient (1:0 to 0:1) to give 10 fractions. Fraction 5 (118.3 mg) was further separated by NP-FCC (11.8 g of silica gel) eluted with CHCl<sub>3</sub>-EtOAc gradient (1:0 to 0:1) to give 6 fractions. Fraction 5-5 (42.3 mg) was separated by ODS-FCC (ϕ 1 cm x 9.5 cm) eluted with H<sub>2</sub>O-MeOH gradient (7:3 to 0:1) to give 4 fractions. Fraction 5-5-2 (22.7 mg) was aspergillide A (**1**). Fraction 5-3 (10.2 mg) was separated by RP-FCC (ϕ 1 cm x 7.0 cm) eluted with H<sub>2</sub>O-MeOH gradient (6:4 to 0:1) to give 6 fractions. Fraction 5-3-3 (2.7 mg) was aspergillide B (**5**). Fraction 4 (114.3 mg) was further separated by FCC (5.0 g of silica gel) eluted with hexane-EtOAc gradient (4:1 to 0:1) into 9 fractions. Fraction 4-3 (52.1 mg) was subjected to preparative TLC developed with hexane/EtOAc (1:1, 3 times development). The band at *R<sub>f</sub>* 0.50 gave fraction 4-3-2 (8.3 mg). Fraction 4-3-2 was further separated by HPLC using an ODS column [Cadenza CD-C18 (ϕ1 cm x 25 cm); flow rate 2.0 mL/min; MeOH/H<sub>2</sub>O (55:45)] into 3 fractions. Fraction 4-3-2-1 (1.9 mg) was pure aspergillide C (**7**).

**Aspergillide A (1):** a colorless oil;  $[\alpha]_D^{27}$  -59.5 (*c* 0.45, CHCl<sub>3</sub>); IR (neat)  $\nu_{\max}$  3421, 2931, 1729, 1436, 1371, 1272, 1205, 1145, 1110, 1051, 1012, 970 cm<sup>-1</sup>; <sup>1</sup>H and <sup>13</sup>C NMR data, see Table 1; HRTOFMS *m/z* 255.1633 [M+H]<sup>+</sup> (calc for C<sub>14</sub>H<sub>23</sub>O<sub>4</sub> 255.1596), 277.1417 [M+Na]<sup>+</sup> (calc for C<sub>14</sub>H<sub>22</sub>O<sub>4</sub>Na 277.1416).

**(R)- and (S)-MTPA Esters (2):** (S)-MTPA chloride (3.3  $\mu$ L; 5.0 eq) was added to a solution of **1** (0.9 mg) in dry pyridine (50  $\mu$ L) at room temperature, and, after 3 h, 3-(dimethylamino)propylamine (3.3  $\mu$ L) was added to convert the excess chloride to a polar amide. After 10 min, the solvent was removed *in vacuo*, and the residue was separated by preparative TLC [benzene/acetone (15:1)], giving (R)-MTPA ester (**2**) (*R<sub>f</sub>* 0.46) (1.3 mg; 78%). Esterification of **1** (0.9 mg) with (R)-MTPA chloride in a similar manner gave (S)-MTPA ester (**2**) (*R<sub>f</sub>* 0.42) (1.5 mg; 90%). (R)-MTPA ester (**2**):  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60-7.34 (5H, m, ArH), 5.81 (1H, br.dd,  $J = 15.1, 7.9$  Hz, H-8), 5.73 (1H, ddd,  $J = 15.1, 8.9, 2.9$  Hz, H-9), 4.97 (1H, m, H-13), 4.92 (1H, m, H-4), 4.38 (1H, br.dd,  $J = 12.9, 4.4$  Hz, H-3), 4.28 (1H, m, H-7), 3.54 (3H, br.s, OMe), 2.67 (1H, dd,  $J = 15.1, 12.9$  Hz, H-2a), 2.49 (1H, dd,  $J = 15.1, 4.4$  Hz, H-2b), 2.30 (1H, br.d,  $J = 15.2$  Hz, H-10a), 2.13 (1H, m, H-6a), 2.122 (1H, m, H-10b), 2.118 (1H, m, H-5a), 1.90 (1H, m, H-12a), 1.87 (1H, m, H-5b), 1.81 (1H, m, H-11a), 1.52 (1H, m, H-11b), 1.45 (1H, m, H-6b), 1.21 (3H, d,  $J = 6.5$  Hz, H-14), 1.20 (1H, m, H-12b) ; HRTOFMS  $m/z$  493.1829  $[\text{M}+\text{Na}]^+$  (calc for  $\text{C}_{24}\text{H}_{29}\text{O}_6\text{F}_3\text{Na}$  493.1814). (S)-MTPA ester (**2**):  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60-7.34 (5H, m, ArH), 5.82 (1H, br.dd,  $J = 15.2, 8.4$  Hz, H-8), 5.73 (1H, ddd,  $J = 15.2, 8.8, 2.7$  Hz, H-9), 4.98 (1H, m, H-13), 4.90 (1H, m, H-4), 4.49 (1H, br.dd,  $J = 13.0, 4.6$  Hz, H-3), 4.29 (1H, m, H-7), 3.59 (3H, br.s, -OMe), 2.69 (1H, dd,  $J = 15.2, 13.0$  Hz, H-2a), 2.51 (1H, dd,  $J = 15.2, 4.6$  Hz, H-2b), 2.31 (1H, br.d,  $J = 14.4$  Hz, H-10a), 2.12 (1H, m, H-10b), 2.058 (1H, m, H-5a), 2.056 (1H, m, H-6a), 1.92 (1H, m, H-12a), 1.83 (1H, m, H-11a), 1.77 (1H, m, H-5b), 1.52 (1H, m, H-11b), 1.38 (1H, m, H-6b), 1.22 (3H, d,  $J = 6.6$  Hz, H-14), 1.21 (1H, m, H-12b) ; HRTOFMS  $m/z$  493.1821  $[\text{M}+\text{Na}]^+$  (calc for  $\text{C}_{24}\text{H}_{29}\text{O}_6\text{F}_3\text{Na}$  493.1814).

**(R)- and (S)-MTPA Esters (4):** A solution of **1** (3.0 mg) and sodium methoxide (6.4 mg; 10 eq) in 100  $\mu$ L MeOH was heated at 45  $^\circ\text{C}$  for 17 h in a sealed tube. The mixture was concentrated, pH of the

solution was adjusted to 2 with 1 M HCl, and extracted with EtOAc (400  $\mu$ L x 2). The organic layer was washed with water (200  $\mu$ L) and brine (200  $\mu$ L), and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was evaporated. The oily residue was dissolved in 200  $\mu$ L of benzene/MeOH (4:1), and the solution was treated with TMS-diazomethane (10% in n-hexane, 39  $\mu$ L; 2 eq) (for methylation of the carboxylic acid produced as a side product) for 10 min. The solvent and the volatile reagent were removed under a reduced pressure to give methyl ester (**3**) (2.6 mg; 77%). The <sup>1</sup>H-NMR spectrum and TLC indicated that this material was pure enough and it was used for the next reaction without purification. **3**: <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  5.64 (1H, dtd,  $J$  = 15.6, 6.8, 0.8 Hz, H-9), 5.51 (1H, ddt,  $J$  = 15.6, 5.6, 1.2 Hz, H-8), 3.695 (1H, m, H-3), 3.691 (1H, m, H-7), 3.49 (1H, m, H-13), 3.37 (3H, s, COOMe), 3.12 (1H, m, H-4), 2.89 (1H, dd,  $J$  = 15.2, 4.0 Hz, H-2a), 2.60 (1H, dd,  $J$  = 15.2, 8.0 Hz, H-2b), 1.92 (2H, m, H-10), 1.75 (1H, m, H-5a), 1.43 (1H, m, H-6a), 1.32 (1H, m, H-6b), 1.27 (1H, m, H-12a), 1.20 (1H, m, H-12b), 1.17 (1H, m, H-5), 0.99 (3H, d,  $J$  = 6.0 Hz, H-14). Chemical shifts of H-11 were undetermined. A 0.5 mg portion of **3** was subjected to esterification with (*S*)-MTPA chloride (0.8  $\mu$ L; 2.3 eq) in pyridine (46  $\mu$ L) at room temperature for 41 h. Work-up in the same manner as described for **2** gave (*R*)-MTPA ester (**4**) (0.6 mg; 69%). (*S*)-MTPA ester (**4**) was also prepared from **3** (1.8 mg) in the same manner (0.4 mg; 13%). (*R*)-MTPA ester (**4**): <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.80-7.05 (5H, m, ArH), 5.50 (1H, br.dt,  $J$  = 15.6, 6.0 Hz, H-9), 5.42 (1H, br.dd,  $J$  = 15.6, 5.3 Hz, H-8), 5.04 (1H, m, H-13), 3.69 (1H, m, H-3), 3.68 (1H, m, H-7), 3.48 (3H, br.s, OMe), 3.37 (3H, s, COOMe), 3.12 (1H, m, H-4), 2.88 (1H, dd,  $J$  = 15.4, 4.0 Hz, H-2a), 2.59 (1H, dd,  $J$  = 15.4, 8.0 Hz, H-2b), 1.74 (2H, m, H-10), 1.42 (1H, m, H-6a), 1.35 (1H, m, H-12a), 1.31 (1H, m, H-6b), 1.17 (1H, m, H-12b), 1.02 (3H, d,  $J$  = 6.3 Hz, H-14). Chemical shifts of H-5 and H-11 were undetermined. HRTOFMS  $m/z$  525.2076 [M+Na]<sup>+</sup> (calc for C<sub>25</sub>H<sub>33</sub>O<sub>7</sub>F<sub>3</sub>Na 525.2076). (*S*)-MTPA ester (**4**): <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.80-

7.05 (5H, m, ArH), 5.55 (1H, br.dt,  $J = 15.8, 6.2$  Hz, H-9), 5.46 (1H, br.dd,  $J = 15.8, 5.2$  Hz, H-8), 5.03 (1H, m, H-13), 3.692 (1H, m, H-3), 3.689 (1H, m, H-7), 3.48 (3H, br.s, OMe), 3.37 (3H, s, COOMe), 3.11 (1H, m, H-4), 2.88 (1H, dd,  $J = 15.3, 4.0$  Hz, H-2a), 2.59 (1H, dd,  $J = 15.3, 8.0$  Hz, H-2b), 1.81 (2H, m, H-10), 1.413 (1H, m, H-6a), 1.410 (1H, m, H-12a), 1.31 (1H, m, H-6b), 1.21 (1H, m, H-12b), 0.99 (3H, d,  $J = 6.2$  Hz, H-14). Chemical shifts of H-5 and H-11 were undetermined. HRTOFMS  $m/z$  525.2070  $[M+Na]^+$  (calc for  $C_{25}H_{33}O_7F_3Na$  525.2076).

**Aspergillide B (5):** a colorless oil;  $[\alpha]_D^{31} -97.2$  (c 0.27, MeOH); IR (neat)  $\nu_{max}$  3440, 2931, 1727, 1257, 1187, 1087, 1025, 925  $cm^{-1}$ ;  $^1H$  and  $^{13}C$  NMR data, see Table S1; HRTOFMS  $m/z$  277.1439 (calc for  $C_{14}H_{22}O_4Na$  277.1416).

**(R)- and (S)-MTPA Esters (6):** (R)-MTPA ester (**6**):  $^1H$ -NMR (400 MHz,  $C_6D_6$ )  $\delta$  7.85-7.00 (5H, m, ArH), 6.12 (1H, br.t,  $J = 15.1$  Hz, H-9), 5.28 (1H, br.d,  $J = 15.1$  Hz, H-8), 5.06 (1H, m, H-13), 4.69 (1H, m, H-4), 4.31 (1H, m, H-7), 4.13 (1H, br.d,  $J = 11.7$  Hz, H-3), 3.45 (3H, br.s, OMe), 2.38 (1H, dd,  $J = 14.1, 11.7$  Hz, H-2a), 2.02 (1H, br.d,  $J = 14.1$  Hz, H-2b), 2.01 (1H, m, H-10a), 1.89 (1H, m, H-6a), 1.72 (1H, m, H-5a), 1.71 (1H, m, H-10b), 1.53 (1H, m, H-12a), 1.52 (1H, m, H-11a), 1.44 (1H, m, H-5b), 1.31 (1H, m, H-11b), 1.26 (1H, m, H-12b), 1.05 (3H, d,  $J = 6.2$  Hz, H-14), 0.98 (1H, br.d,  $J = 10.5$  Hz, H-6b); HRTOFMS  $m/z$  471.2017  $[M+H]^+$  (calc for  $C_{24}H_{30}O_6F_3$  471.1994), 493.1820  $[M+Na]^+$  (calc for  $C_{24}H_{29}O_6F_3Na$  493.1814). (S)-MTPA ester (**6**):  $^1H$ -NMR (400 MHz,  $C_6D_6$ )  $\delta$  7.85-7.00 (5H, m, ArH), 6.12 (1H, br.t,  $J = 15.1$  Hz, H-9), 5.25 (1H, br.d,  $J = 15.1$  Hz, H-8), 5.08 (1H, m, H-13), 4.73 (1H, m, H-4), 4.26 (1H, m, H-7), 4.16 (1H, br.d,  $J = 10.6$  Hz, H-3), 3.45 (3H, br.s, OMe), 2.61 (1H, dd,  $J = 13.6, 10.6$  Hz, H-2a), 2.15 (1H, br.d,  $J = 13.6$  Hz, H-2b), 1.99 (1H, m, H-10a), 1.72 (1H, m, H-6a), 1.70 (1H, m, H-10b), 1.61 (1H, m, H-5a), 1.57 (1H, m, H-12a), 1.52 (1H, m, H-11a), 1.37 (1H, m, H-5b), 1.298 (1H, m, H-12b), 1.297 (1H, m, H-11b), 1.06 (3H, d,  $J = 6.1$  Hz, H-14), 0.87 (1H, br.d,  $J = 13.9$  Hz, H-

12b); HRTOFMS  $m/z$  471.2009  $[M+H]^+$  (calc for  $C_{24}H_{30}O_6F_3$  471.1994), 493.1810  $[M+Na]^+$  (calc for  $C_{24}H_{29}O_6F_3Na$  493.1814).

**Aspergillide C (7):** a colorless oil;  $[\alpha]_D^{25} +66.2$  ( $c$  0.19, MeOH); IR (neat)  $\nu_{max}$  3278, 2931, 1720, 1419, 1365, 1288, 1033, 971  $cm^{-1}$ ;  $^1H$  and  $^{13}C$  NMR data, see Table 3; HRTOFMS  $[(M+Na)^+ m/z$  275.1260, calc for  $C_{14}H_{20}O_4Na$  275.1259]

**(R)- and (S)-MTPA (8):** (R)-MTPA ester (**8**):  $^1H$ -NMR (400 MHz,  $C_6D_6$ )  $\delta$  7.80-7.10 (5H, m, ArH), 5.95 (1H, ddd,  $J = 10.0, 5.6, 2.0$  Hz, H-5), 5.86 (1H, dddd,  $J = 16.0, 10.0, 6.0, 2.0$  Hz, H-9), 5.57 (1H, dd,  $J = 10.0, 3.6$  Hz, H-6), 5.12 (1H, m, H-13), 5.10 (1H, dd,  $J = 16.0, 4.4$  Hz, H-8), 4.70 (1H, dd,  $J = 5.6, 2.4$  Hz, H-4), 4.15 (1H, ddd,  $J = 11.2, 2.0, 2.0$  Hz, H-3), 3.49 (3H, br.s, OMe), 2.54 (1H, dd,  $J = 14.0, 11.2$  Hz, H-2a), 2.03 (1H, dd,  $J = 14.0, 1.6$  Hz, H-2b), 1.95 (1H, m, H-10a), 1.59 (1H, m, H-10b), 1.54 (1H, m, H-12), 1.44 (1H, m, H-11a), 1.31 (1H, m, H-12a), 1.16 (1H, m, H-11b), 1.04 (3H, d,  $J = 6.8$  Hz, H-14); HRTOFMS  $m/z$  491.1640  $[M+Na]^+$  (calc for  $C_{24}H_{27}O_6F_3Na$  491.1657). (S)-MTPA ester (**8**):  $^1H$ -NMR (400 MHz,  $C_6D_6$ )  $\delta$  7.80-7.10 (5H, m, ArH), 5.85 (1H, m, H-5), 5.84 (1H, m, H-9), 5.50 (1H, dddd,  $J = 10.4, 6.0, 3.6, 2.4$  Hz, H-6), 5.16 (1H, m, H-13), 5.07 (1H, br.d,  $J = 14.4$  Hz, H-8), 4.78 (1H, ddd,  $J = 5.6, 2.4, 2.0$  Hz, H-4), 4.19 (1H, ddd,  $J = 11.6, 4.0, 2.0$  Hz, H-3), 3.40 (3H, br.s, OMe), 2.78 (1H, ddd,  $J = 14.0, 11.6, 2.8$  Hz, H-2a), 2.19 (1H, ddd,  $J = 14.0, 2.0, 2.4$  Hz, H-2b), 1.94 (1H, m, H-10a), 1.56 (1H, m, H-10b), 1.50 (1H, m, H-12), 1.44 (1H, m, H-11a), 1.35 (1H, m, H-12a), 1.16 (1H, m, H-11b), 1.04 (3H, dd,  $J = 6.8, 2.8$  Hz, H-14); HRTOFMS  $m/z$  491.1672  $[M+Na]^+$  (calc for  $C_{24}H_{27}O_6F_3Na$  491.1657).

**Furan Product (9):** A solution of **5** (1.0 mg) and sodium methoxide (2.1 mg; 10 eq) in 100  $\mu$ L MeOH was sealed and heated at 57  $^{\circ}C$  for 48 h. The solvent was removed and 1  $M$  HCl was added to the

residue until pH of the solution was 3. The aqueous mixture was extracted with EtOAc (1 mL), and the organic layer was washed with water (1 mL) and brine (1 mL). The oily residue, obtained after drying over Na<sub>2</sub>SO<sub>4</sub>, filtration, and concentration, was dissolved in 200  $\mu$ L of benzene/acetone (4:1). The solution was treated with TMS-diazomethane (10% in n-hexane, 20  $\mu$ L; 1.2 eq), and after 10 min the mixture was concentrated to give **9** (0.9 mg; 81%): <sup>1</sup>H-NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  6.26 (1H, dt,  $J$  = 16.0, 6.8 Hz, H-9), 6.15 (1H, br.d,  $J$  = 16.0 Hz, H-8), 5.98 (1H, d,  $J$  = 3.2 Hz, H-6), 5.90 (1H, br.d,  $J$  = 3.2 Hz, H-5), 3.50 (1H, m, H-13), 3.31 (3H, s, COOMe), 2.86 (2H, br.t,  $J$  = 7.6 Hz, H-3), 2.41 (2H, t,  $J$  = 7.6 Hz, H-2), 2.05 (2H, br.td,  $J$  = 6.9, 6.8 Hz, H-10), 1.50-1.20 (3H, m, H-11, 12, overlap), 0.99 (3H, d,  $J$  = 6.0 Hz, H-14); <sup>13</sup>C-NMR (100 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  172.1 (C-1), 159.6 (C-4), 152.9 (C-7), 126.9 (C-8), 128.5 (C-9), 111.9 (C-6), 107.7 (C-5), 68.5 (C-13), 51.0 (OMe), 39.0 (C-12), 33.6 (C-2), 33.0 (C-10), 26.5 (C-3), 25.8 (C-11), 23.7 (C-14); HRTOFMS  $m/z$  289.1418 [M+Na]<sup>+</sup> (calc for C<sub>15</sub>H<sub>22</sub>O<sub>4</sub>Na 289.1416).

**(R)- and (S)-MTPA Esters (10):** (R)-MTPA ester (**10**): <sup>1</sup>H-NMR (700 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.80-7.10 (5H, m, ArH), 6.11 (1H, dt,  $J$  = 15.4, 7.0 Hz, H-9), 6.05 (1H, d,  $J$  = 15.4 Hz, H-8), 5.97 (1H, d,  $J$  = 3.5 Hz, H-5), 5.90 (1H, d,  $J$  = 3.5 Hz, H-6), 5.05 (1H, m, H-13), 3.47 (3H, s, COOMe), 3.31 (3H, br.s, OMe), 2.86 (2H, t,  $J$  = 7.7 Hz, H-3), 2.40 (2H, t,  $J$  = 7.7 Hz, H-2), 1.86 (2H, dt,  $J$  = 7.0, 7.0 Hz, H-10), 1.36 (1H, m, H-12a), 1.17 (1H, m, H-12b), 1.16 (2H, m, H-11), 1.01 (3H, d,  $J$  = 3.6 Hz, H-15); HRTOFMS  $m/z$  505.1814 [M+Na]<sup>+</sup> (calc for C<sub>25</sub>H<sub>29</sub>O<sub>6</sub>F<sub>3</sub>Na 505.1814). (S)-MTPA ester (**10**): <sup>1</sup>H-NMR (700 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  7.80-7.10 (5H, m, ArH), 6.16 (1H, dt,  $J$  = 16.1, 7.0 Hz, H-9), 6.09 (1H, d,  $J$  = 16.1 Hz, H-8), 5.98 (1H, d,  $J$  = 2.8 Hz, H-5), 5.90 (1H, d,  $J$  = 2.8 Hz, H-6), 5.03 (1H, m, H-13), 3.46 (3H, s, COOMe), 3.31 (3H, br.s, OMe), 2.86 (2H, t,  $J$  = 7.0 Hz, H-3), 2.40 (2H, t,  $J$  = 7.0 Hz, H-2), 1.92 (1H, dt,  $J$  = 7.0,



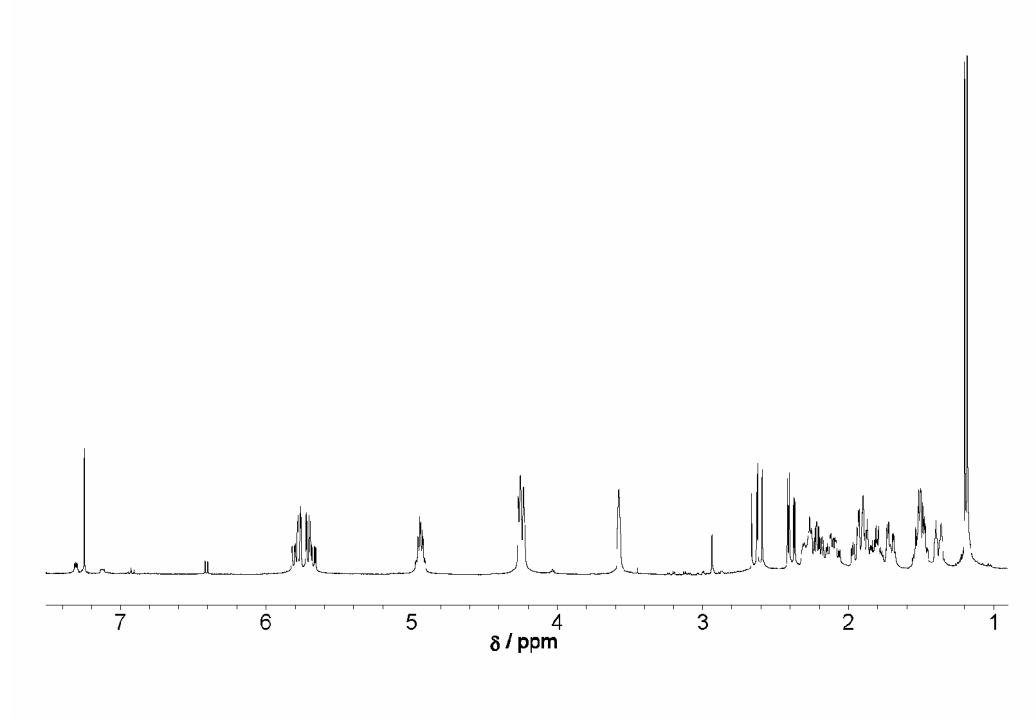
7.0 Hz, H-10), 1.42 (1H, m, H-12a), 1.26 (2H, m, H-11), 1.22 (1H, m, H-12b), 0.97 (3H, d,  $J = 3.6$  Hz, H-14); HRTOFMS  $m/z$  505.1813  $[M+Na]^+$  (calc for  $C_{25}H_{29}O_6F_3Na$  505.1814).

**Table S1.** NMR data (C<sub>6</sub>D<sub>6</sub>, 400/100 MHz) of aspergillide B (**5**)<sup>a</sup>

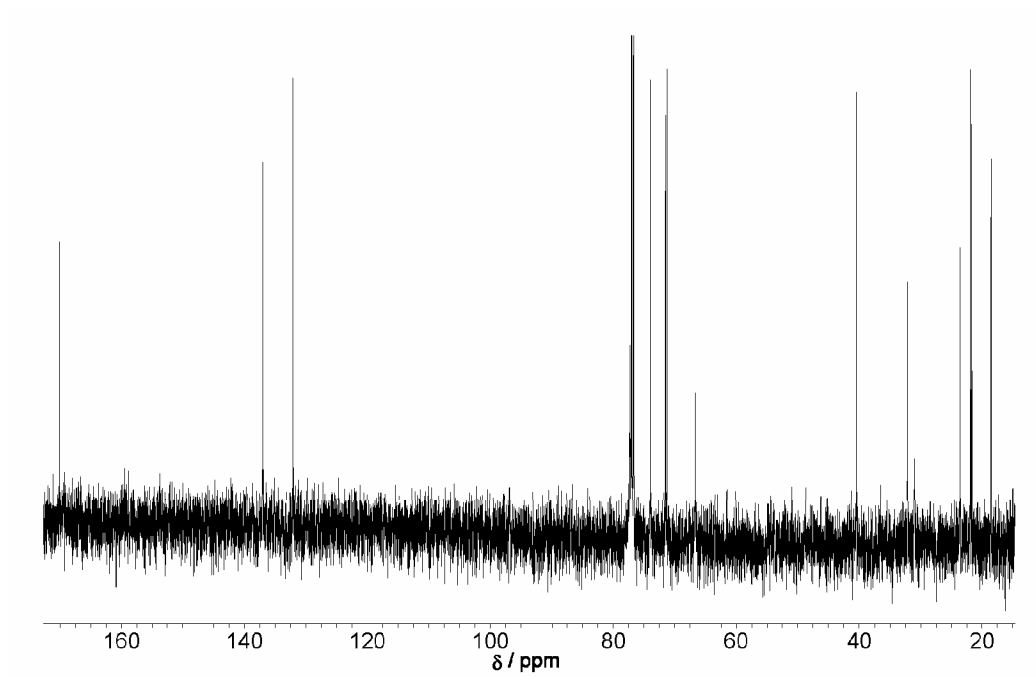
	$\delta_{\text{C}}$ , mult.	$\delta_{\text{H}}$ ( <i>J</i> in Hz)	COSY	HMBC
1	169.8, C			
2	39.9, CH <sub>2</sub>	2.71, dd (13.7, 11.3)	3	1, 3
		2.12, dd (13.7, 1.8)	3	1, 3, 4
3	69.8, CH	4.08, br.d, (11.3)	2	1, 2, 4, 7
4	67.2, CH <sub>2</sub>	3.22, br.d, (10.4)	5, 4-OH	
5	27.8, CH <sub>2</sub>	1.55, m	4, 6	3, 6
		1.37, m	4, 6	6
6	22.6, CH <sub>2</sub>	1.78, m	5, 7	4, 5, 7
		0.99, dddd, (13.9, 4.9, 2.7, 1.2)	5	4, 5
7	71.5, CH	4.30, m	6, 8, 9	3, 5, 8
8	129.0, CH	5.38, br.dd (15.8, 4.3)	7, 9	6, 7, 10
9	138.2, CH	6.19, dddd (15.8, 10.8, 4.9, 1.9)	8, 10	7, 10
10	30.7, CH <sub>2</sub>	2.04, dddd, (13.3, 10.8, 4.9, 1.9)	9, 11	11, 12
		1.74, m	9, 11	8, 11, 12
11	25.3, CH <sub>2</sub>	1.52, m	10, 12	10, 12, 13
		1.34, m	10, 12	12, 13
12	32.1, CH <sub>2</sub>	1.61, m	11, 13	10, 11, 13, 14
		1.31, m	11, 13	10, 11, 13, 14
13	69.6, CH	5.09, m	12, 14	11
14	19.2, CH <sub>3</sub>	1.07, d, (6.3)	13	12, 13
4-OH		1.88, d, (10.4)	4	3, 4

<sup>a</sup> Carbon multiplicities were based on a DEPT experiment.

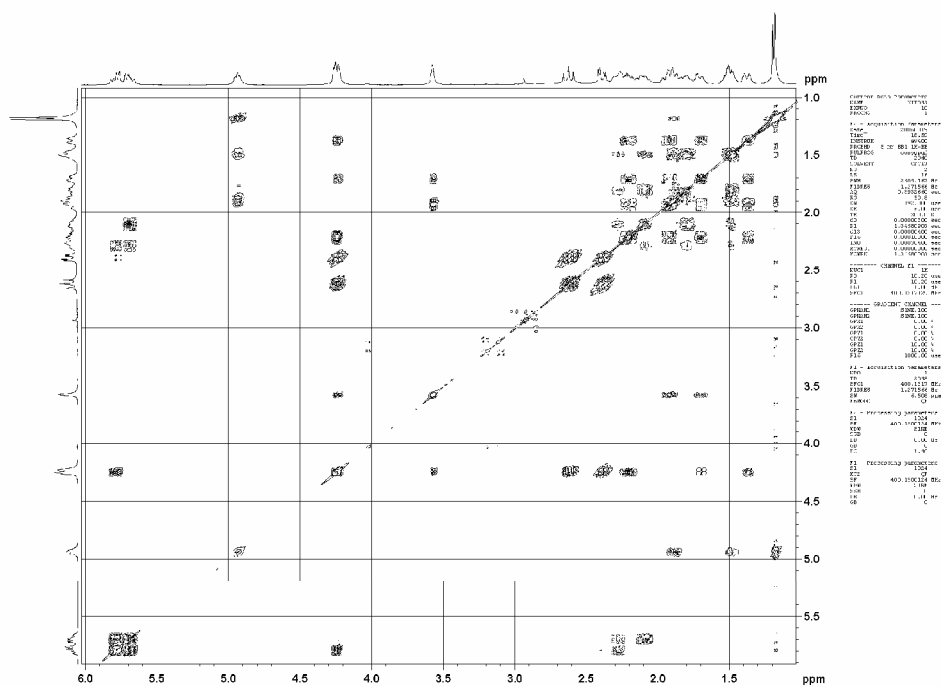
**Figure S1.**  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ) of aspergillide A (**1**).



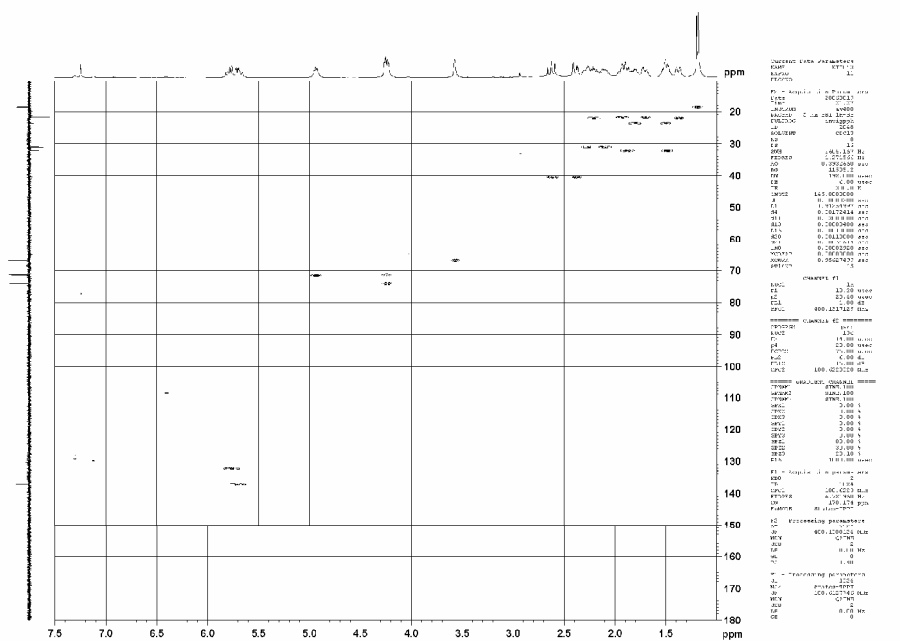
**Figure S2.**  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ) of aspergillide A (**1**).



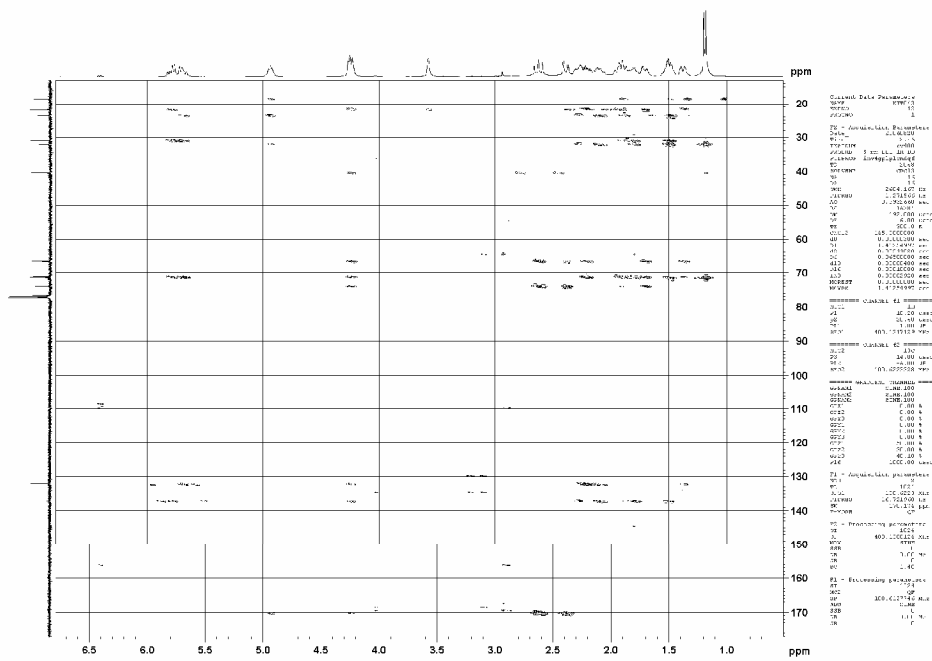
**Figure S3.**  $^1\text{H}$ - $^1\text{H}$  COSY (400 MHz,  $\text{CDCl}_3$ ) spectrum of aspergillide A (**1**).



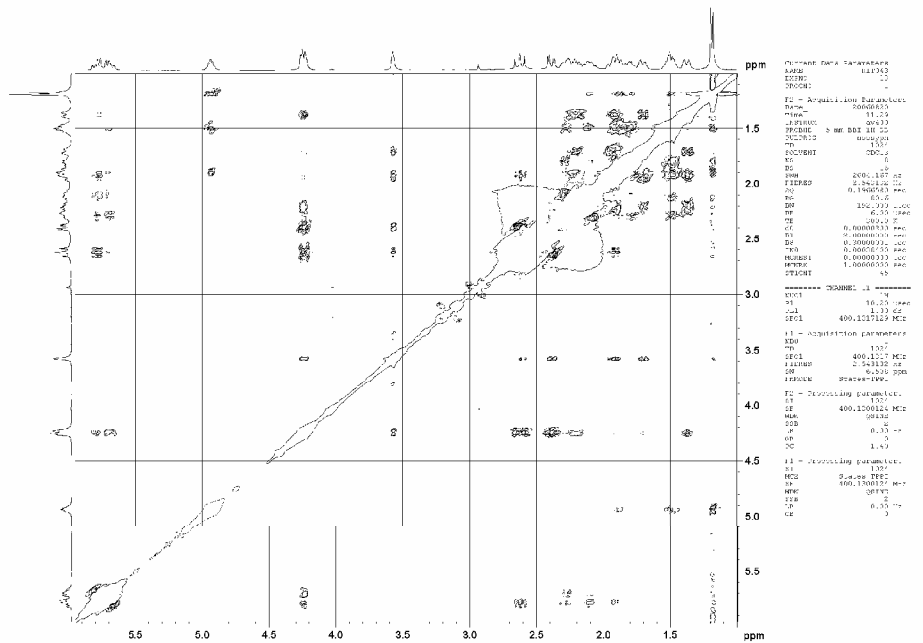
**Figure S4.** HSQC (400 MHz,  $\text{CDCl}_3$ ) spectrum of aspergillide A (**1**).



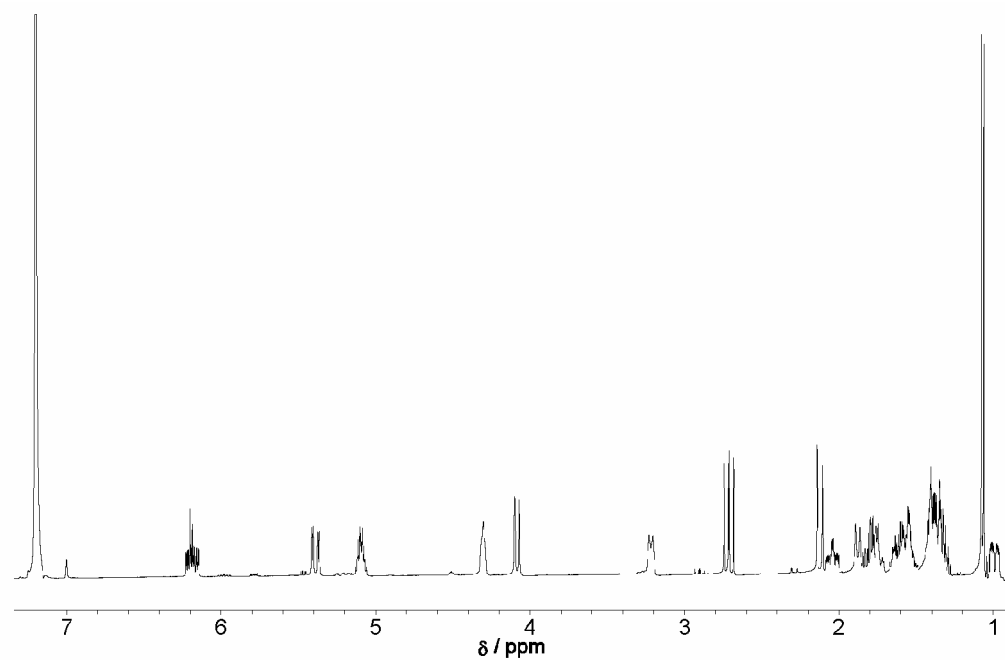
**Figure S5.** HMBC (400 MHz, CDCl<sub>3</sub>) spectrum of aspergillide A (**1**).



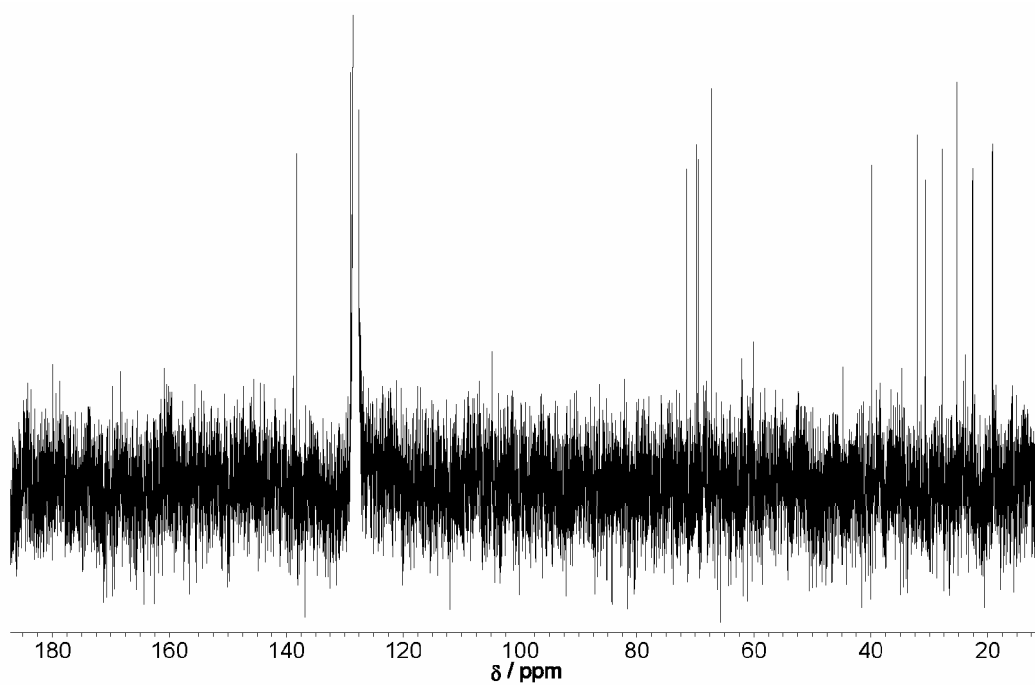
**Figure S6.** NOESY (400 MHz, CDCl<sub>3</sub>) spectrum of aspergillide A (**1**).



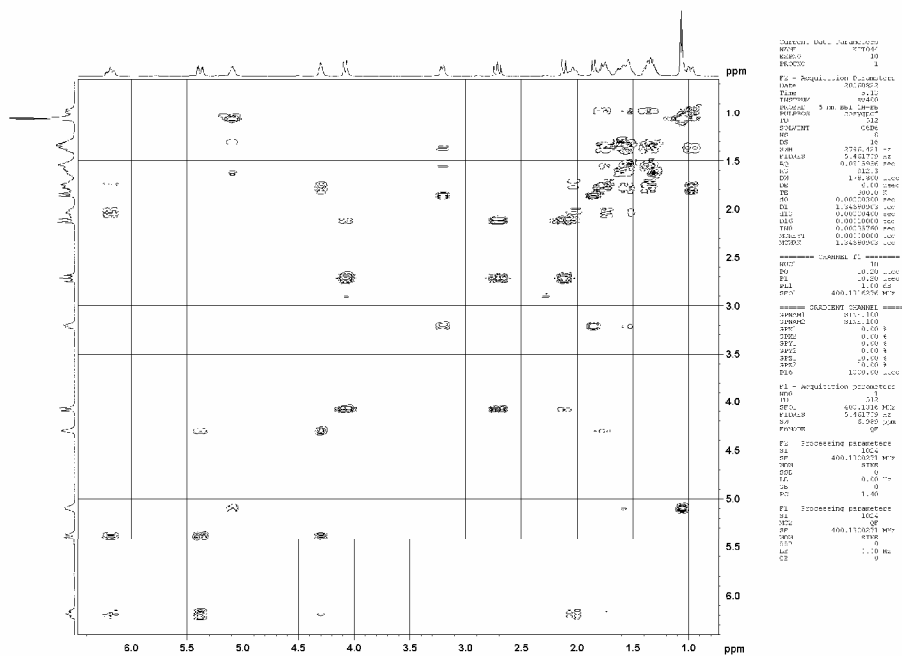
**Figure S7.**  $^1\text{H}$ -NMR (400 MHz,  $\text{C}_6\text{D}_6$ ) of aspergillide B (**5**).



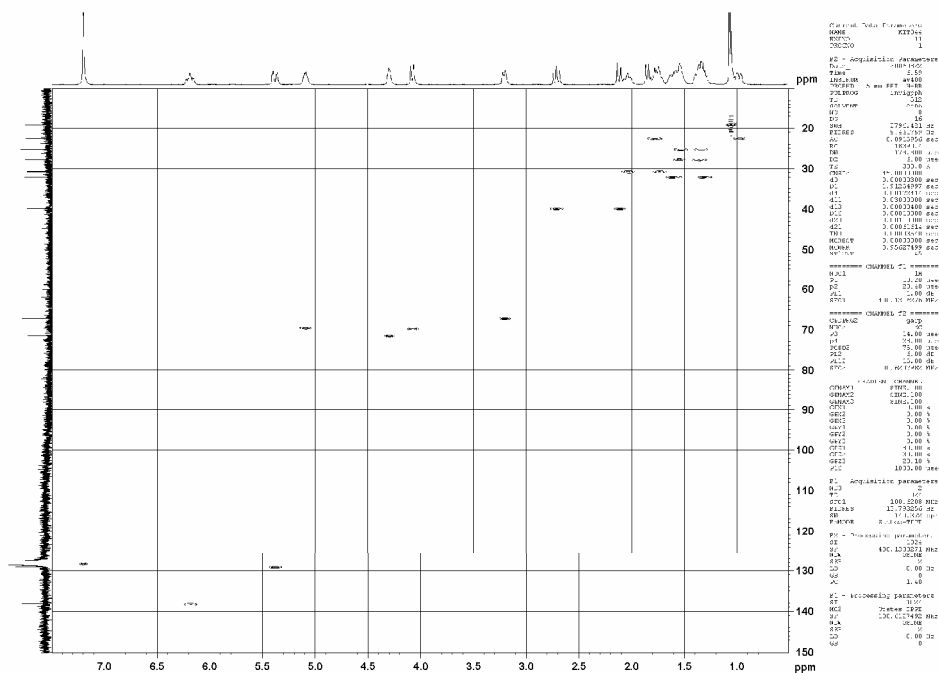
**Figure S8.**  $^{13}\text{C}$ -NMR (100 MHz,  $\text{C}_6\text{D}_6$ ) of aspergillide B (**5**).



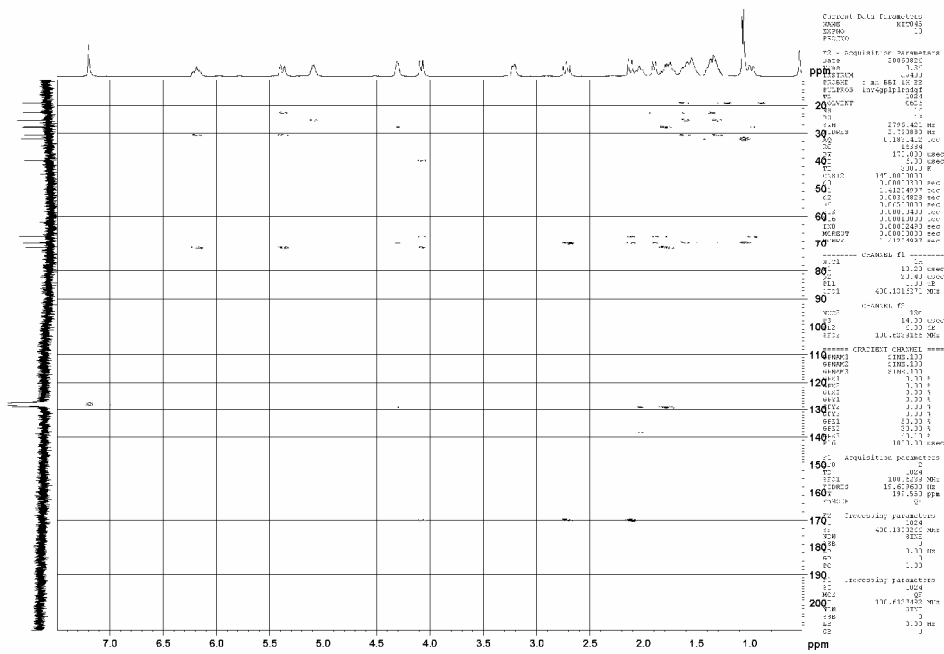
**Figure S9.**  $^1\text{H}$ - $^1\text{H}$  COSY (400 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of aspergillide B (**5**).



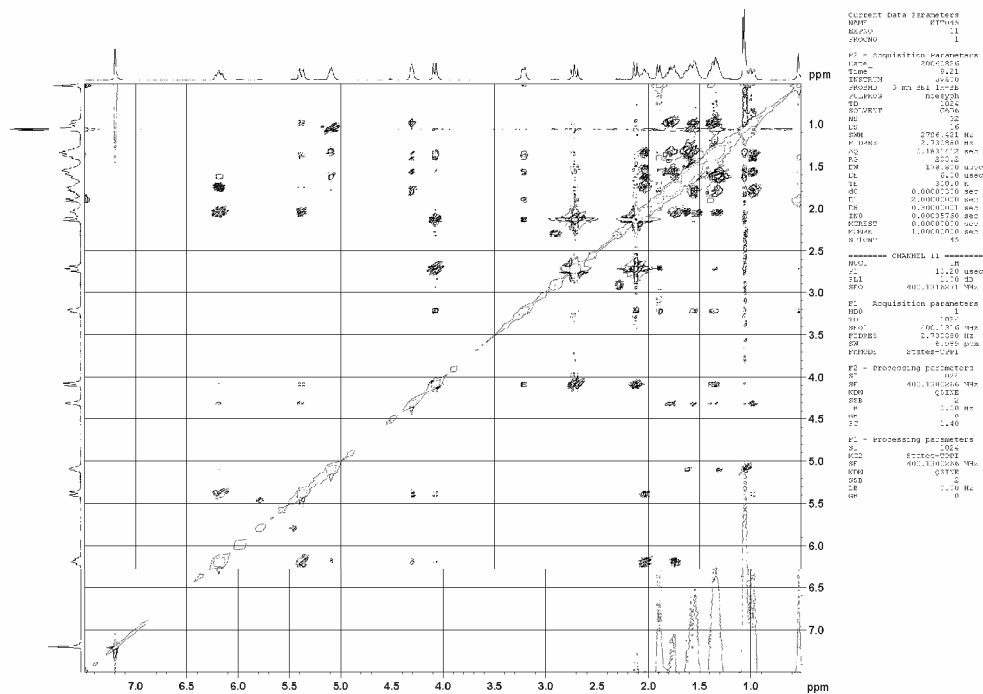
**Figure S10.** HSQC (400 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of aspergillide B (**5**).



**Figure S11.** HMBC (400 MHz, C<sub>6</sub>D<sub>6</sub>) spectrum of aspergillide B (**5**).

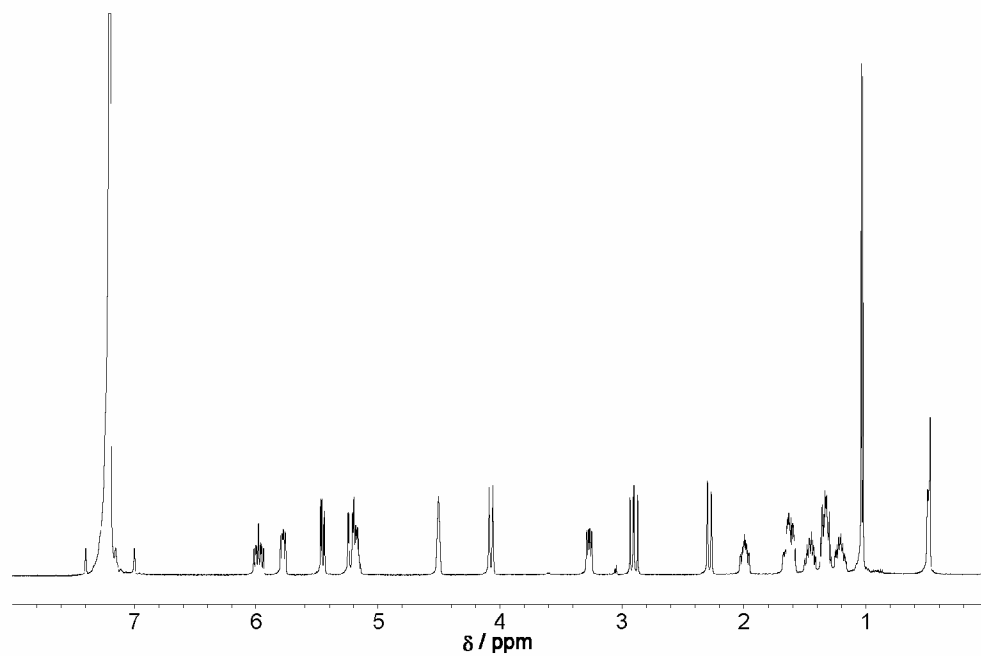


**Figure S12.** NOESY (400 MHz, C<sub>6</sub>D<sub>6</sub>) spectrum of aspergillide B (**5**).

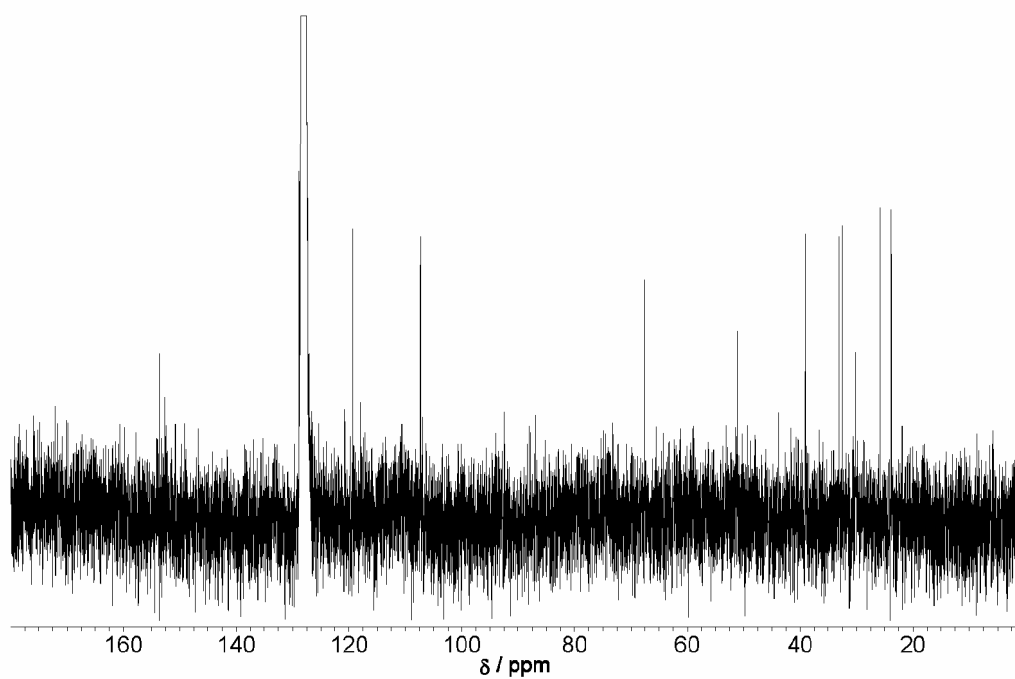




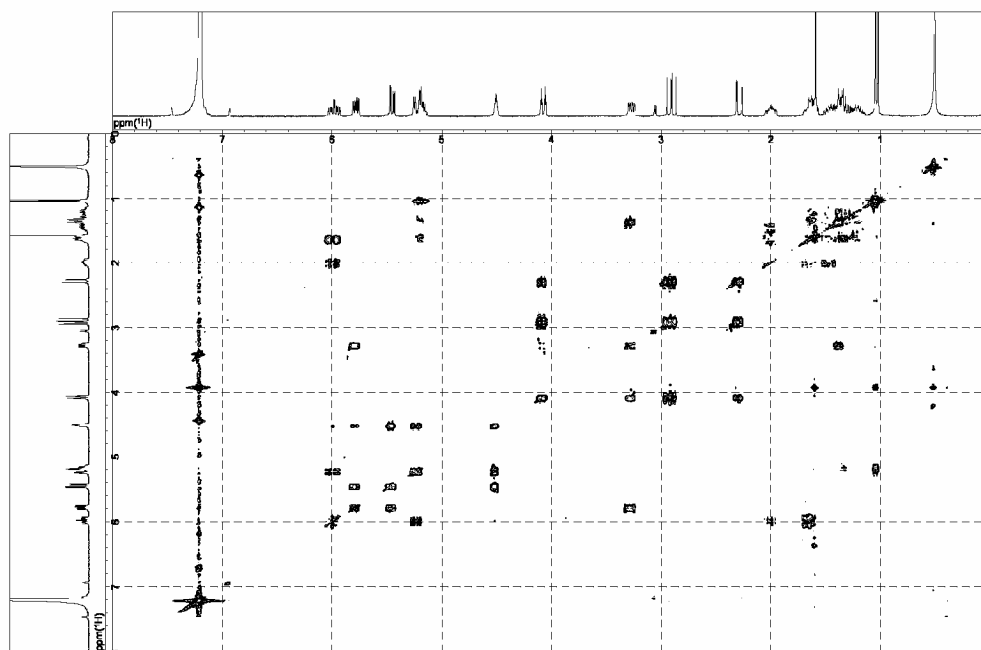
**Figure S13.**  $^1\text{H}$ -NMR (400 MHz,  $\text{C}_6\text{D}_6$ ) of aspergillide C (**7**).



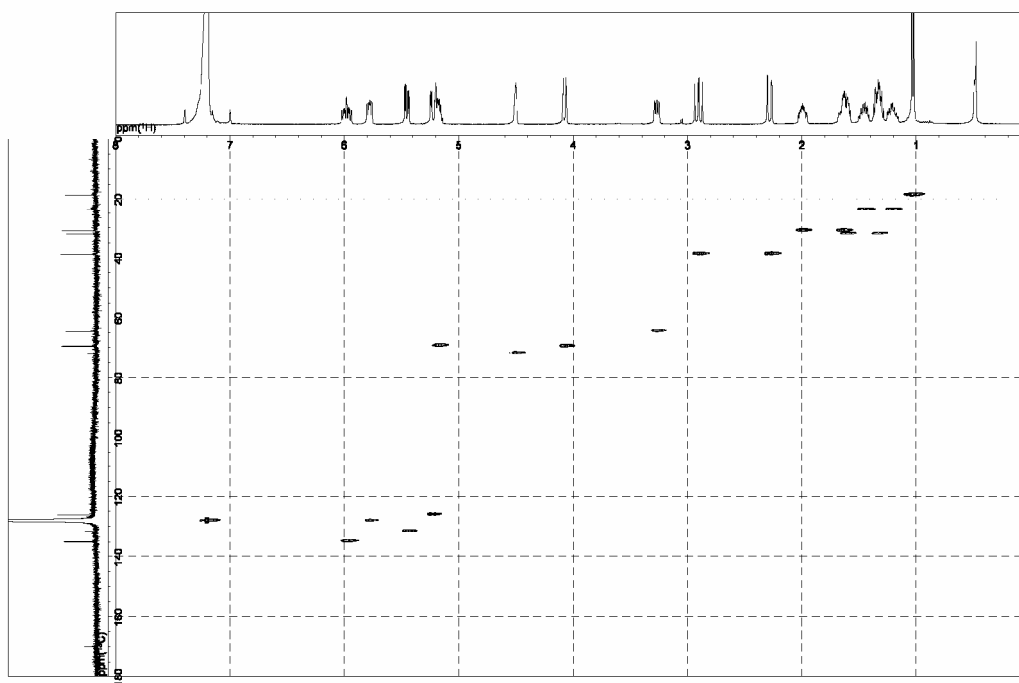
**Figure S14.**  $^{13}\text{C}$ -NMR (100 MHz,  $\text{C}_6\text{D}_6$ ) of aspergillide C (**7**).



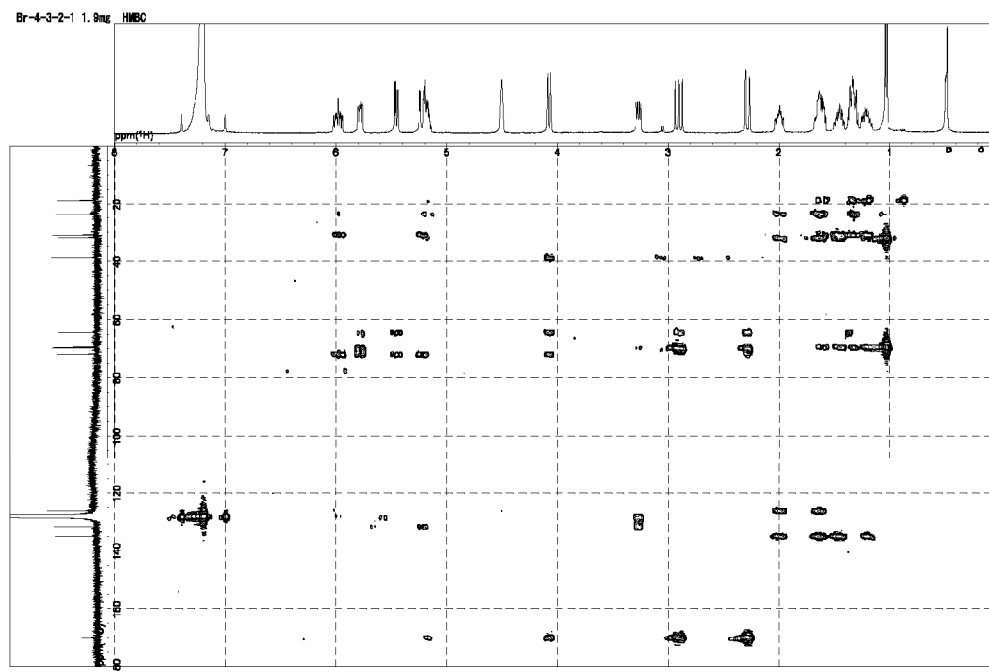
**Figure S15.**  $^1\text{H}$ - $^1\text{H}$  COSY (400 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of aspergillide B (7).



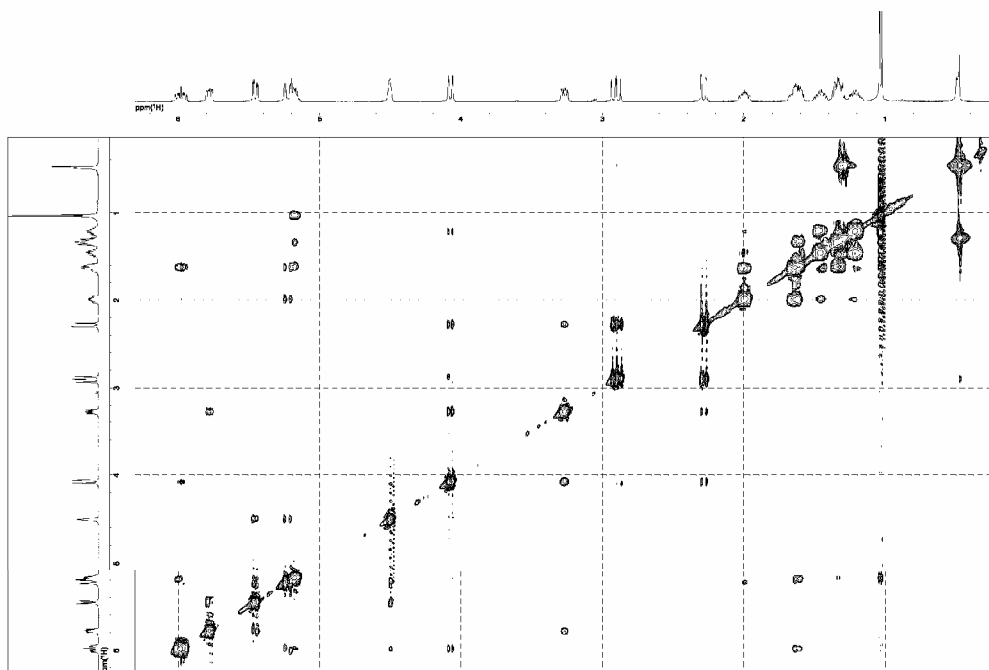
**Figure S16.** HSQC (400 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of aspergillide C (7).



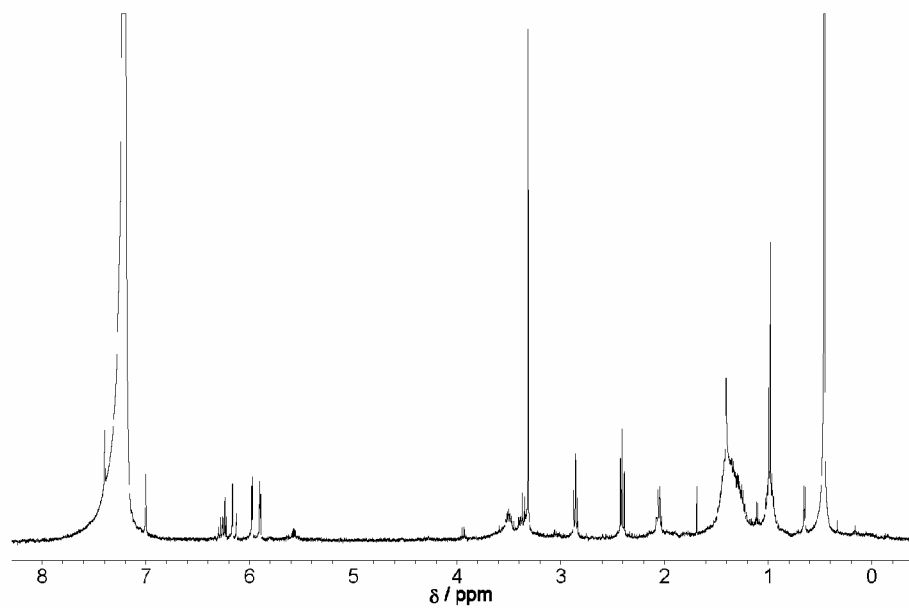
**Figure S17.** HMBC (400 MHz, C<sub>6</sub>D<sub>6</sub>) spectrum of aspergillide C (**7**).



**Figure S18.** NOESY (400 MHz, C<sub>6</sub>D<sub>6</sub>) spectrum of aspergillide C (**7**).



**Figure S19.**  $^1\text{H}$ -NMR (400 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of furan product (**9**).



**Figure S20.**  $^{13}\text{C}$ -NMR (100 MHz,  $\text{C}_6\text{D}_6$ ) spectrum of furan product (**9**).

