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Hypoxylonols C–F, Benzo[*j*]fluoranthenes from *Hypoxylon truncatum*

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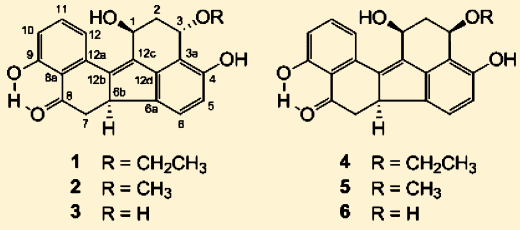
Supporting Information

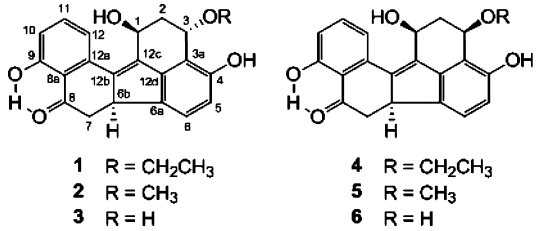
ABSTRACT: Four novel benzo[*j*]fluoranthene derivatives, hypoxylonols C (**3**), D (**4**), E (**5**), and F (**6**), have been isolated from the mushroom *Hypoxylon truncatum*, together with two known benzo[*j*]fluoranthene derivatives, hypoxylonols A (**1**) and B (**2**). The structures were established by analysis of NMR spectroscopic data and X-ray diffraction data. Compounds **4** and **5** showed antiproliferative activity against HUVECs (human umbilical vein endothelial cells) and HUAECs (human umbilical artery endothelial cells).



Tumor angiogenesis plays an important role in the growth of tumor cells and involves several steps such as proliferation, migration, invasion, and tubular formation of vascular endothelial cells. These processes are regulated by multiple factors such as vascular endothelial growth factor (VEGF) and its receptor (VEGFR). Tumor angiogenesis inhibitors represent a promising strategy for the treatment of cancer. We have isolated the novel compounds hypochromins A and B as antiangiogenic agents from the marine-derived fungus *Hypocrea vinosa*[1] and boletopsin C as a KDR (VEGFR-2) inhibitor from the mushroom *Boretopsis leucomelas*.[2]

We have previously reported two benzo[*j*]fluoranthene derivatives, hypoxylonols A (**1**) and B (**2**), from *Hypoxylon truncatum* (Schweinitz:Fries) J. H. Miller (Xylariaceae), an inedible mushroom.[3] Asakawa isolated truncatone, a benzo[*j*]fluoranthene derivative from the fruiting bodies of this mushroom.[4] The cytotoxic benzo[*j*]fluoranthenes, daldinones C and D, were isolated from solid culture of the endophyte *H. truncatum* (strain no. IFB-18).[6] Ten additional natural benzo[*j*]fluoranthene derivatives have been reported.[5−10]

In this paper, we report the isolation and structure determination of six benzo[*j*]fluoranthene derivatives from the fruiting bodies of *H. truncatum*. The planar structures of four novel benzo[*j*]fluoranthene derivatives (**3**–**6**) were determined by spectroscopic analysis (the planar structures of **1** and **2** were reported previously[3]), and the absolute configurations of **1**–**6** were determined by NMR spectroscopic analysis and X-ray diffraction analysis. The proliferation inhibitory activity of these compounds was also evaluated against human umbilical vein endothelial cells (HUVECs) and human umbilical artery endothelial cells (HUAECs).



RESULTS AND DISCUSSION

The powdered fruiting bodies of *H. truncatum* were extracted with $CHCl_3$. The $CHCl_3$ extract showed antiproliferative activity against HUVECs. Bioactivity-guided fractionation of the $CHCl_3$ extract afforded six benzo[*j*]fluoranthene derivatives, hypoxylonols A (**1**), B (**2**), C (**3**), D (**4**), E (**5**), and F (**6**).

The known compounds **1** and **2** were identified as hypoxylonols A and B, respectively, by comparing their spectroscopic profiles (NMR, UV, IR, MS) with published data.[3] The planar structures of **1** and **2** have been already reported, but the stereochemistry has not. Hypoxylonol B (**2**) was crystallized as yellow platelets from *n*-hexane/acetone, and its absolute configuration was determined by X-ray diffraction analysis. The absolute configurations of C-1, C-3, and C-6b were determined to be *S*, *S*, and *R*, respectively, which were deduced from the Flack parameter, −0.05(11), refined using 2907 Friedel pairs (Figure 1). The ^1H and ^{13}C NMR spectra of hypoxylonol A (**1**) were very similar to those of **2**.[3] The main difference between **1** and **2** was the replacement of an ethoxy group with a methoxy group at C-3.

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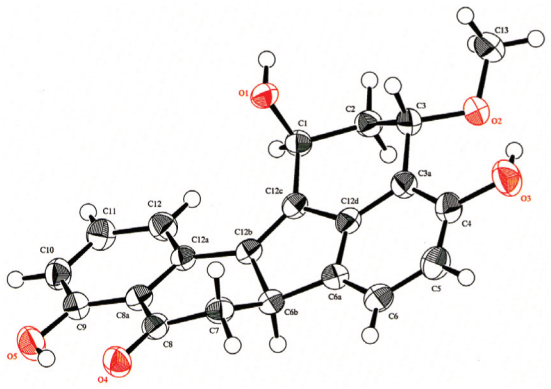

Figure 1. ORTEP drawing of **2** obtained by X-ray analysis. [Flack parameter: $x = -0.05(11)$].

Hypoxylonol C (**3**) was crystallized as pale yellow needles from *n*-hexane/acetone. The molecular formula of **3** was determined to be $C_{20}H_{16}O_5$ on the basis of HRFABMS. The IR spectrum showed absorption peaks at 3375 cm^{-1} (hydroxyl group), 3250 cm^{-1} (hydroxyl group), and 1630 cm^{-1} (carbonyl group). The ^1H and ^{13}C NMR (Table 1) and HMQC spectra of **3** revealed the presence of two methylenes, three sp^3 methines, two of which were attached to oxygen, five sp^2 methines, nine sp^2 quaternary carbons, two of which were attached to oxygen, one carbonyl carbon, and four hydroxyl groups, one of which was chelated. Inspection of the $^1H-^1H$ coupling constants and $^1H-^1H$ COSY indicated the proton sequences from H-1 to H-3, H-5 to H-6, H-6b to H-7, and H-10 to H-12. The signals at δ_H 4.27, 5.14, 8.60, and 12.59 were assigned to the hydroxyl protons attached to C-1, C-3, C-4, and C-9 based on HMBC correlations. The HMBC correlations of H-1 to C-12d, H-2 to C-3a and C-12c, O*H*-4 to C-3a, H-5 to C-4 and C-6a, and H-6 to C-12d established the presence of a hydronaphthalene ring. The HMBC correlations of H-6b to C-12b, H-7 to C-8 and C-8a, H-10 to C-8a and C-9, H-11 to C-12a, and H-12 to C-12b established the presence of another hydronaphthalene ring. These two hydronaphthalene rings were connected at C-6a and C-6b on the basis of HMBC correlations of H-6 to C-6b and H-7 to C-6a. Considering the molecular formula, carbon C-12b was connected to C-12c.

To determine the absolute stereochemistry of C-1, C-3, and C-6b, **3** was subjected to X-ray diffraction analysis. The absolute configurations of C-1, C-3, and C-6b of **3** were determined to be *S*, *S*, and *R*, respectively, which were deduced from the Flack parameter, −0.09(16), refined using 1367 Friedel pairs.

The molecular formula of hypoxylonol D (**4**) was determined to be $C_{22}H_{20}O_5$ on the basis of HREIMS. The IR spectrum showed absorption peaks at 3400 cm^{-1} (hydroxyl group)

Table 1. NMR Spectroscopic Data [400 (^1H) and 100 (^{13}C) MHz, acetone-d_6] for Compounds 3−6

	hypoxylonol C (**3**)		hypoxylonol D (**4**)		hypoxylonol E (**5**)		hypoxylonol F (**6**)	
position	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)
1	62.7	5.59 dd (8.5, 4.3)	64.3	5.35 m	64.2	5.35 m	65.1	5.37 d (8.5)
2	42.3	2a: 2.46 dt (13.1, 4.3)	38.5	2a: 2.41 dt (13.4, 4.4)	38.0	2a,b: 2.38 m	43.3	2a: 2.47 dt (12.6, 4.4)
		2b: 2.14 ddd (13.1, 8.5, 3.2)		2b: 2.34 dt (13.4, 6.3)				2b: 2.25 dt (12.6, 8.5)
3	65.4	5.47 m	73.1	5.15 dd (6.3, 4.4)	74.5	5.02 dd (5.9,3.9)	67.0	5.36 d (8.5)
3a	120.5		118.7		118.4		120.7	
4	155.7		155.3		155.3		155.4	
5	114.3	6.67 d (8.0)	114.3	6.72 d (7.8)	114.3	6.72 d (8.1)	114.4	6.68 d (8.0)
6	123.4	7.28 d (8.0)	124.0	7.31 d (7.8)	124.1	7.31 d (8.1)	123.6	7.28 d (8.0)
6a	136.4		136.7		136.7		136.4	
6b	49.7	4.10 dd (13.9, 5.6)	49.6	4.06 dddd (13.9, 5.6, 1.7,0.7)	49.5	4.05 dddd (13.9, 5.5, 1.7,0.7)	50.0	4.10 dddd (13.8, 5.5, 24, 0.7)
7	43.6	7a: 3.37 dd (16.4, 5.6)	43.4	7a: 3.39 dd (164, 5.6)	43.3	7a: 3.38 dd (16.4, 5.5)	43.6	7a: 3.39 dd (16.5, 5.5)
		7b: 2.30 dd (16.4, 13.9)		7b: 2.36 dd (16.4, 13.9)		7b: 2.35 dd (16.4, 13.9)		7b: 2.33 dd (16.5, 13.8)
8	205.8		205.8		205.7		205.7	
8a	115.5		115.6		115.6		115.6	
9	163.5		163.5		163.5		163.3	
10	117.0	6.83 dd (7.9, 1.2)	116.9	6.82 dd (7.8, 1.5)	117.0	6.82 dd (7.7, 1.5)	116.8	6.81 dd (7.9, 1.3)
11	137.4	7.54 t (7.9)	137.1	7.54 t (7.8)	137.1	7.53 t (7.7)	136.9	7.52 t (7.9)
12	118.8	7.48 dd (7.9, 1.2)	119.8	7.50 dd (7.8, 1.5)	119.7	7.49 dd (7.7, 1.5)	120.7	7.47 dd (7.9, 1.3)
12a	139.4		139.1		139.1		139.2	
12b	137.6		137.6		137.7		137.3	
12c	138.0		138.8		138.7		138.8	
12d	144.0		144.2		144.2		144.0	
1-OH		4.27 s		4.25 d (7.1)		4.16 d (7.1)		
3-OH		5.14 brd (4.2)						
4-OH		8.60 s		8.54 s		8.50 s		
9-OH		12.59 s		12.60 s		12.60 s		12.58 s
3-OCH_3					56.9	3.51 s		
3-O$CH_2$$CH_3$			65.1	a: 3.86 dq (9.3, 7.0)				
				b: 3.72 dq (9.3, 7.0)				
3-OCH$_2$$CH_3$			15.9	1.22 t (7.0)				

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and 1620 cm^{-1} (carbonyl group). The ^1H and ^{13}C NMR (Table 1) and HMQC spectra of **4** revealed the presence of one methyl, three methylenes, three sp^2 methines, two of which were attached to oxygen, five sp^2 methines, nine sp^2 quaternary carbons, two of which were attached to oxygen, one carbonyl carbon, and three hydroxyl groups, one of which was chelated. The ^1H and ^{13}C NMR data of **4** were similar to those of **1**, and the $^1H-^1H$ COSY and HMBC correlations suggested that **4** has the benzo[*j*]fluoranthene skeleton. The methyl proton δ_H 1.22 showed an HMQC correlation with the methyl carbon δ_C 15.9. The methylene protons δ_H 3.72 and 3.86 showed HMQC correlations with the methylene carbon δ_C 65.1, which was attached to oxygen. The $^1H-^1H$ COSY spectrum indicated the proton sequence from δ_H 1.22 to δ_H 3.72 and 3.86. These data suggested the presence of one ethoxyl group. The HMBC correlations of δ_H 3.86 and 3.72 to δ_C 73.1 and δ_H 5.15 to δ_C 65.1 revealed that the ethoxyl group was attached to C-3. Since the ^{13}C NMR chemical shifts of the C-2 and C-3 positions of **4** were different from those of **1**, **4** was considered to be a stereoisomer of **1**, which differs in the stereochemistry of C-3.

The molecular formula of hypoxylonol E (**5**) was found to be $C_{21}H_{18}O_5$ by HREIMS. The IR spectrum showed absorption peaks at 3375 cm^{-1} (hydroxyl group) and 1630 cm^{-1} (carbonyl group). The ^1H and ^{13}C NMR (Table 1) and HMQC spectra of **5** revealed the presence of one methyl, two methylenes, three sp^3 methines, two of which were attached to oxygen, five sp^2 methines, nine sp^2 quaternary carbons, two of which were attached to oxygen, one carbonyl carbon, and three hydroxyl groups, one of which was chelated. These data were very similar to those of **2**. The $^1H-^1H$ COSY and HMBC correlations suggested that **5** also had the benzo[*j*]fluoranthene skeleton. The HMBC correlations of δ_H 3.51 to δ_C 74.5 and δ_H 5.02 to δ_C 56.9 revealed that the methoxyl group was attached to C-3. Since the ^{13}C NMR chemical shifts of the C-2, C-3, and C-12d positions of **5** were different from those of **2**, **5** was considered to be a stereoisomer of **2**. Compound **5** was obtained as yellow block crystals from *n*-hexane/$CHCl_3$/MeOH, which allowed the structure to be determined by X-ray diffraction analysis. The absolute configurations of C-1, C-3, and C-6b were determined to be *S*, *R*, and *R*, respectively, which were deduced from the Flack parameter, 0.0(2), refined using 6313 Friedel pairs. The ^1H and ^{13}C NMR spectra of **4** were very similar to those of **5**. The main difference between **4** and **5** was the replacement of an ethoxy group with a methoxy group at C-3.

The molecular formula of hypoxylonol F (**6**) was found to be $C_{20}H_{16}O_5$ by HREIMS *m*/*z* 337.1074 $[M + H]^+$. The IR spectrum showed absorption peaks at 3375 cm^{-1} (hydroxyl group) and 1630 cm^{-1} (carbonyl group). The ^1H and ^{13}C NMR spectra of **6** (Table 1) were very similar to those of **3**, and 2D NMR data established that **6** had the same planar structure as **3**. Since the ^{13}C NMR chemical shifts of the C-1, C-2, C-3, and C-12 positions of **6** were different from those of **3**, **6** was considered to be a stereoisomer of **3**. Compound **6** was obtained as yellow block crystals from *n*-hexane/acetone, which allowed the structure to be determined by X-ray diffraction analysis. The absolute configurations of C-1, C-3, and C-6b were determined to be *S*, *R*, and *R*, respectively, which were deduced from the Flack parameter, 0.07(14), refined using 1326 Friedel pairs. The CD spectra of compounds **1** and **4** were similar to those of compounds **2**, **3**, **5**, and **6** (Supporting Information). The absolute configurations of compounds **1** and **4**, except for C-3, are suggested to be the same as those of compounds **2**, **3**, **5**, and **6**.

We tested the proliferation inhibitory activity of **1**−**6** against HUVECs and HUAECs in the MTT assays. Compounds **4** and **5** showed antiproliferative activity against HUVECs with IC_{50} values of 6.9 and 7.4 μM, respectively. Compounds **4** and **5** also showed antiproliferative activity against HUAECs with IC_{50} values of 6.1 and 4.1 μM, respectively (Table 2). Proliferation of vascular endothelial cells is required as the first step in tumor angiogenesis. The result suggests that compounds **4** and **5** have the potential to be novel antitumor angiogenic agents.

Table 2. Growth Inhibition of Compounds 1−6 against HUVECs and HUAECs

	IC_{50} (μM)	
compound	HUVECs	HUAECs
1	15	16
2	24	24
3	21	16
4	6.9	6.1
5	7.4	4.1
6	17	14

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were determined on a Yanaco MP apparatus. Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were recorded with a Shimadzu UV-240 spectrophotometer. Circular dichroism (CD) measurements were carried out on a Jasco 820 spectropolarimeter. IR spectra were recorded with a Jasco IR Report-100 spectrophotometer. ^1H NMR and ^{13}C NMR spectra were measured with a JEOL JNM-AL400 MHz spectrometer in acetone-d_6. Chemical shift values were reported in δ values (ppm) relative to the internal solvent reference of ^1H [δ 2.04] and ^{13}C [δ 29.8], respectively. Low- and high-resolution EIMS and FABMS spectra were measured with a JEOL JMS-700 spectrometer. Column chromatography was performed using silica gel 60N (Kanto Chemical), Sephadex LH-20 (GE Healthcare), and PEGASIL PREP ODS-7515-12-A (Senshu Scientific Co., Ltd.). HPLC was performed on a Senshu flow system SSC-3461 equipped with a SSC-5410 UV/vis detector at 254 nm, with an ODS [PEGASIL ODS (10 ⌀ × 250 mm, no. 340096)] column.

Fungal Material. Fruiting bodies were collected in Higashikurume, Tokyo, Japan, in September 2009. A voucher specimen (KI-2009-HK1) was deposited at the Department of Pharmacognosy and Phytochemistry, Meiji Pharmaceutical University. The fungus was derived from the spores of the fruiting bodies and was identified by rDNA sequence analysis. The internal transcribed spacer regions 1 and 2 and 5.8 rDNA in the rRNA gene of the fungus were identical to those of *Hypoxylon truncatum* (accession number: AF201716).

Extraction and Isolation. The dried and powdered fruiting bodies of *H. truncatum* (402 g) were extracted successively with $CHCl_3$, MeOH, and acetone at room temperature. The $CHCl_3$ extract (15.9 g) showed antiproliferative activity against HUVECs with an IC_{50} value of 10 μg/mL and was used for the bioassay-guided fractionation and isolation of compounds. The $CHCl_3$ extract was subjected to step-gradient silica gel column chromatography with a solvent system consisting of 0−100% MeOH/$CHCl_3$ to yield five fractions (fractions A−E). Fraction D (5.1 g, IC_{50} = 9.4 μg/mL) was subjected to step-gradient silica gel column chromatography with a solvent system consisting of 0−100% MeOH/$CHCl_3$ to yield five fractions (fractions D1−D5). Fraction D2 (IC_{50} = 2.1 μg/mL) was subjected to step-gradient ODS CC with a solvent system consisting of 50−100% H_2O/MeOH to yield six fractions (fractions D2-1−D2-6), two of which were hypoxylonols B (**2**) (31.8 mg) (fraction D2-2) and D (**4**) (34.2 mg) (fraction D2-5). Fraction D2-4 (IC_{50} = 6.1 μg/mL) was subjected to reversed-phase HPLC with 58% MeOH to afford hypoxylonols A (**1**) (36.7 mg) and E (**5**) (26.9 mg). Fraction D4 was dissolved with $CHCl_3$ to afford

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hypoxylonol C (**3**) (664.8 mg) as the insoluble part. The soluble part (IC_{50} = 6.5 μg/mL) was subjected to three chromatography steps: (1) Sephadex LH-20 CC with MeOH; (2) step-gradient silica gel CC with 0−100% $CHCl_3$/MeOH; and (3) reversed-phase ODS HPLC with 75% MeOH to afford **3** (38.4 mg) and hypoxylonol F (**6**) (77.1 mg).

Cell Culture. HUVECs and HUAECs were purchased from Lonza Walkersville, Inc., and cultured using EGM-2 Bulletkit (Lonza Walkersville, Inc.) and EGM-2MV Bulletkit (Lonza Walkersville, Inc.), respectively, at 37 °C in 5% CO_2.

Growth Inhibition Assay. HUVECs (3000 cells/well) and HUAECs (3000 cells/well) were seeded in collagen-coated 96-well plates with EGM-2 and EGM-2MV Bulletkits, respectively, for 3 h at 37 °C in 5% CO_2. The medium was removed and replaced with 1% FBS-EBM-2 and incubated for 21 h at 37 °C in 5% CO_2. VEGF (1 nM) and tested samples were added to each well and incubated for 72 h at 37 °C in 5% CO_2. Ki8751 was used as a positive control (IC_{50} = 1.0−2.0 μM). Cell proliferation was detected using WST-8 reagent, and the inhibition of proliferation was measured at an absorbance at 450 nm using a plate reader.

*Hypoxylonol C (**3**):* pale yellow needles; mp 183 °C (dec); $[\alpha]^{21}_D$ −13.3 (*c* 0.30, acetone); UV (acetone) λ_{max} (log ε) 210 (4.15), 316 (3.53), 326 (3.67), 387 (3.94) nm; IR (KBr) ν_{max} 3375, 3250, 1630, 1460, 1240, 1035, 810, 750 cm^{-1}; ^1H NMR (acetone-d_6) see Table 1; ^{13}C NMR (acetone-d_6) see Table 1; FABMS *m*/*z* 335 $[M - H]^-$; HRFABMS *m*/*z* 335.0925 $[M - H]^-$ (calcd for $C_{20}H_{15}O_5$, 335.0919).

*Hypoxylonol D (**4**):* yellow powder; mp 152−154 °C; $[\alpha]^{21}_D$ −24.5 (*c* 0.27, acetone); UV (acetone) λ_{max} (log ε) 210 (4.19), 319 (3.76), 326 (3.65), 388 (4.00) nm; IR (KBr) ν_{max} 3400, 2925, 1620, 1460, 1360, 1320, 1070, 810 cm^{-1}; ^1H NMR (acetone-d_6) see Table 1; ^{13}C NMR (acetone-d_6) see Table 1; EIMS *m*/*z* 364 $[M]^+$ (20), 318 (100), 301 (20), 300 (67), 290 (22); HREIMS *m*/*z* 364.1308 $[M]^+$ (calcd for $C_{22}H_{20}O_5$, 364.1311).

*Hypoxylonol E (**5**):* yellow block crystals; mp 160−162 °C; $[\alpha]^{21}_D$ −41.2 (*c* 0.29, acetone); UV (acetone) λ_{max} (log ε) 210 (4.20), 320 (3.77), 326 (3.68), 389 (4.01) nm; IR (KBr) ν_{max} 3375, 2925, 1630, 1460, 1370, 1330, 1230, 1060, 805 cm^{-1}; ^1H NMR (acetone-d_6) see Table 1; ^{13}C NMR (acetone-d_6) see Table 1; EIMS *m*/*z* 350 $[M]^+$ (38), 318 (100), 300 (64); HREIMS *m*/*z* 350.1156 $[M]^+$ (calcd for $C_{21}H_{18}O_5$, 350.1154).

*Hypoxylonol F (**6**):* yellow block crystals; mp 187 °C (dec); $[\alpha]^{21}_D$ −19.8 (*c* 0.25, acetone); UV (acetone) λ_{max} (log ε) 210 (4.16), 320 (3.58), 326 (3.69), 388 (3.97) nm; IR (KBr) ν_{max} 3375, 1630, 1460, 1215, 1050 cm^{-1}; ^1H NMR (acetone-d_6) see Table 1; ^{13}C NMR (acetone-d_6) see Table 1; FABMS *m*/*z* 337 $[M + H]^+$; HRFABMS *m*/*z* 337.1074 $[M + H]^+$ (calcd for $C_{20}H_{17}O_5$, 337.1076).

Single-Crystal X-ray Crystallographic Analysis. All measurements were obtained using a Rigaku RAXIS RAPID diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.54187 Å). The structures of **2**, **3**, **5**, and **6** were solved by direct methods (SHELX97) and expanded using Fourier techniques (DIRDIF99).

*Crystal Data for **2**.* Hypoxylonol B (**2**) was crystallized from *n*-hexane/acetone to give yellow platelets. A single crystal of dimensions 0.25 × 0.10 × 0.03 mm^3 was used for X-ray measurements. Crystal data: $C_{21}H_{18}O_5$, space group $P2_1$ (#4), *a* = 8.90851(16) Å, *b* = 15.3789(3) Å, *c* = 12.3961(9) Å, β = 102.989(7)°, *V* = 1654.86(12) $Å^3$, *Z* = 4, D_{calc} = 1.406 g/cm^3, R1 = 0.0314, wR2 = 0.0810.

*Crystal Data for **3**.* Hypoxylonol C (**3**) was crystallized from *n*-hexane/acetone to give pale yellow needles. A single crystal of dimensions 0.25 × 0.10 × 0.05 mm^3 was used for X-ray measurements. Crystal data: $C_{23}H_{22}O_6$, space group $P2_12_12_1$ (#19), *a* = 5.68762(10) Å, *b* = 13.5860(3) Å, *c* = 24.1080(17) Å, *V* = 1862.87(14) $Å^3$, *Z* = 4, D_{calc} = 1.406 g/cm^3, R1 = 0.0313, wR2 = 0.0792.

*Crystal Data for **5**.* Hypoxylonol E (**5**) was crystallized from *n*-hexane/$CHCl_3$/MeOH to give yellow block crystals. A single crystal of dimensions 0.16 × 0.08 × 0.05 mm^3 was used for X-ray measurements. Crystal data: $C_{85}H_{82.78}O_{24.39}$, space group $P2_1$ (#4), *a* = 8.4841(6) Å, *b* = 35.0879(6) Å, *c* = 12.7693(9) Å, β = 109.561(8)°, *V* = 3581.9(4) $Å^3$, *Z* = 2, D_{calc} = 1.386 g/cm^3, R1 = 0.0847, wR2 = 0.2310.

*Crystal Data for **6**.* Hypoxylonol F (**6**) was crystallized from *n*-hexane/acetone to give yellow block crystals. A single crystal of dimensions 0.10 × 0.08 × 0.05 mm^3 was used for X-ray measurements. Crystal data: $C_{20}H_{16}O_5$, space group $P2_1$ (#4), *a* = 5.2050(3) Å, *b* = 18.0275(10) Å, *c* = 8.0225(6) Å, β = 92.299(7)°, *V* = 752.17(8) $Å^3$, *Z* = 2, D_{calc} = 1.485 g/cm^3, R1 = 0.0353, wR2 = 0.0897.

The supplementary crystallographic data for **2**, **3**, **5** and **6** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre, under the reference numbers CCDC 784644, 777234, 784645, and 784646, respectively. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 1223 336033 or e-mail: data_request@ccdc.cam.ac.uk.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

$^1H/^{13}C$ NMR, 2D NMR spectra, CD spectra, ORTEPs, and CIF files of compounds are available free of charge via the Internet at http://pubs.acs.org.

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