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Synthesis and Absolute Configuration of Hongoquercin B, a Sesquiterpene-substituted Orsellinic Acid Isolated as a Fungal Metabolite†

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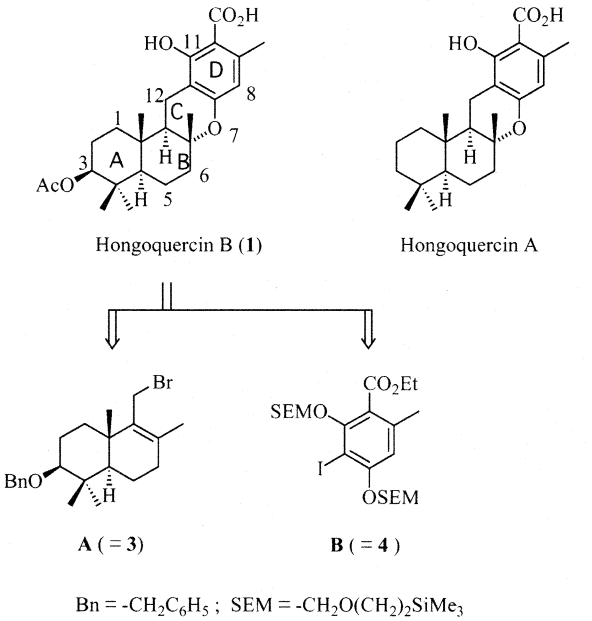
(+)-Hongoquercin B (1), a weakly antibacterial fungal metabolite, was synthesized by starting from (*S*)-3-hydroxy-2,2-dimethylcyclohexanone, and its absolute configuration was determined as depicted by structure 1.

Key words: configuration determination; heterocycles; hongoquercin B; terpenoids; total synthesis

In 1998, Roll *et al.* isolated (+)-hongoquercin B together with (+)-hongoquercin A from an unidentified terrestrial fungus as a metabolite which was slightly active against vancomycin-resistant *Enterococcus faecium*.[1] Their extensive NMR study on hongoquercin B enabled them to propose structure **1** for it, although its absolute configuration remained unknown. We have recently synthesized (+)-hongoquercin A and determined its absolute configuration as depicted in Scheme 1.[2] Since hongoquercin B is a congener of hongoquercin A, its absolute configuration may be the same as that of hongoquercin A. It must be verified, however, whether or not **1** is the correct absolute configuration of hongoquercin B. We therefore decided to synthesize **1**. Prior to the development of the successful route that is subsequently detailed, we attempted to use olefin cyclization reactions to construct the ring system of **1** from acyclic sesquiterpene precursors. All of our attempts unfortunately resulted in failure, and we therefore planned our synthesis as shown in Scheme 1. The present retrosynthetic analysis is essentially the same as that employed for the synthesis of hongoquercin A.[2] Sesquiterpene building block **A** is a known compound, which was reported by Mori and Koga in 1995,[3] while orsellinic acid block **B** was prepared in our hongoquercin A work.[2]

Scheme 2 summarizes the synthesis of (+)-hongoquercin B (**1**). (*S*)-3-Hydroxy-2,2-dimethylcyclohexanone (**C**), which was readily available by reducing the corresponding diketone with baker's yeast,[4] was converted in a 6% yield in 12 steps to bicyclic alcohol **2**. Displacement of the primary hydroxy group of **2** with a bromine atom gave corresponding bromide **3**[3] which served as sesquiterpene building block **A**. Building block **B** (=**4**) was prepared from ethyl orsellinate as previously reported.[2]

Lithiation of **4** with 1 equiv. of butyllithium at −78°C furnished the 3-lithiate which was treated with copper (I) cyanide to give the corresponding cuprate. This cuprate smoothly reacted with bromide **3**, and the product was chromatographed to give crude **5** contaminated with the bis[2-(trimethylsilyl)ethoxymethyl (bisSEM) ether of ethyl orsellinate that had been generated by protonolysis of the



Scheme 1. Structure and Retrosynthetic Analysis of (+)-Hongoquercin B (**1**).

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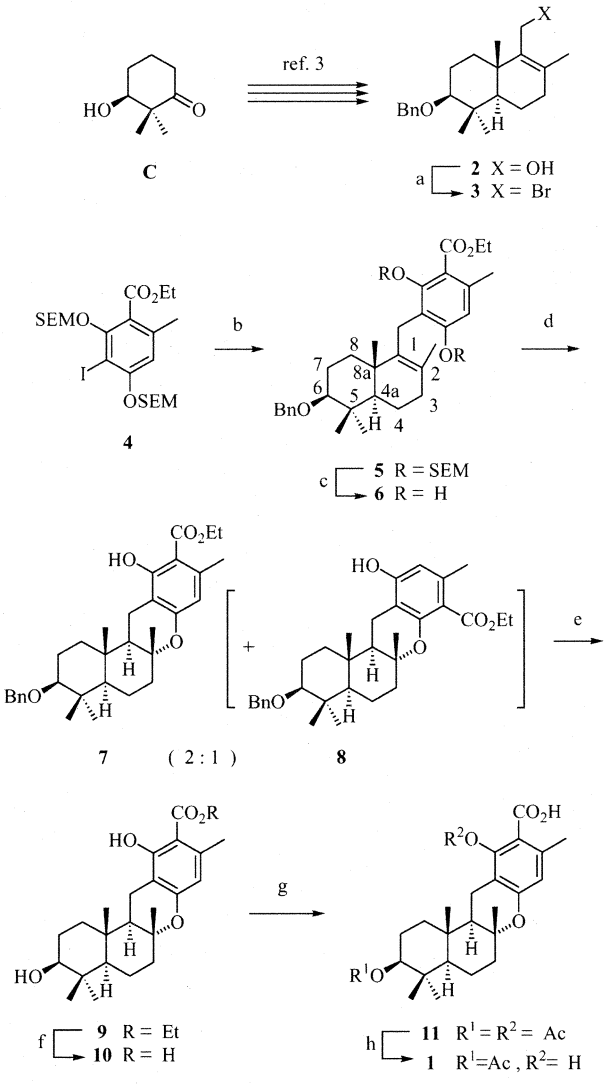
cuprate. The SEM protective groups were then removed from crude **5** by treating with sulfuric acid in ethanol and THF to give, after chromatographic purification, dihydroxy ester **6** in a 74% yield based on **2**.

Ring closure of **6** to **7** was executed by employing boron trifluoride-diethyl ether in dichloromethane as the catalyst to give a mixture of **7** and **8** (2:1). Fortunately **8**, which showed a strong IR absorption at 3380 cm^{-1} due to the non-hydrogen-bonded phenolic hydroxy group, was much more soluble in ethanol than desired product **7** with a weak IR absorption at 3340 cm^{-1} due to the hydrogen-bonded phenolic hydroxy group. Accordingly, recrystallization of the crude product from ethanol furnished **7** in a 58% yield. Removal of the benzyl protective group of **7** was achieved by conventional palladium-catalyzed hydrogenolysis to give hydroxy ester **9**. The stereostructure of **9** was carefully checked by an NMR analysis. Figure 1 summarizes the important ^{1}H- and ^{13}C-NMR data for **9**. The assigned stereochemistry as depicted by **9** is supported by the similarity between the NMR data for **9** and those for hongoquercin A ethyl ester, together with NOESY correlations between the various protons of **9**. It should be added that the structure of (±)-hongoquercin A ethyl ester had been firmly established by an X-ray crystallographic analysis.[2)]

Conversion of **9** to hongoquercin B (**1**) was achieved in three steps. Firstly, **9** was treated with potassium hydroxide to afford acid **10**. In order to confirm the absolute configuration of **10**, we measured and compared its CD spectrum with that of (+)-hongoquercin A. As shown in Fig. 2, the spectra were virtually identical, indicating that they had the



Scheme 2. Synthesis of (+)-Hongoquercin B. Reagents: (a) PBr_3, Et_2O (quant.); (b) BuLi, THF; CuCN; **3**; (c) H_2SO_4, THF, EtOH (74% based on **2**); (d) $BF_3 \cdot OEt_2$, CH_2Cl_2 (58% of **7**, 27% of **8**); (e) H_2, Pd–C, EtOAc (93%); (f) (i) KOH, THF, MeOH, H_2O; (ii) H_3O+ (96%); (g) Ac_2O, C_5H_5N; (h) K_2CO_3, MeOH, H_2O (89% based on **10**).

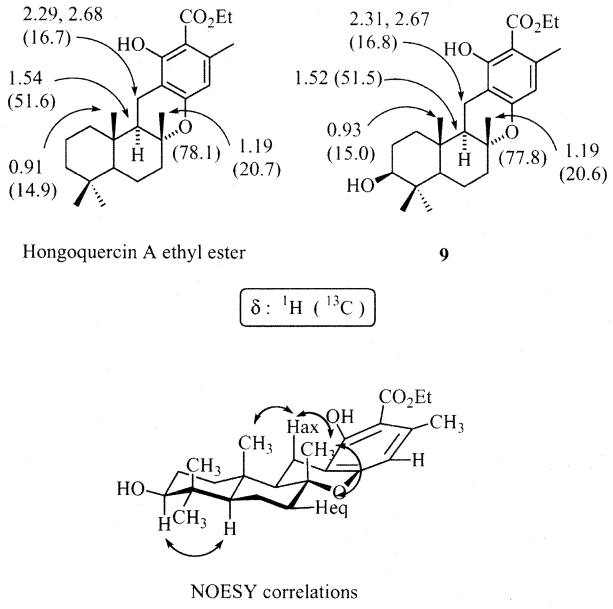


Fig. 1. NMR Data for **9** [^{1}H-NMR at 500 MHz, ^{13}C-NMR at 125 MHz, as $CDCl_3$ Solution].
^{13}C chemical shift values are shown in parentheses.

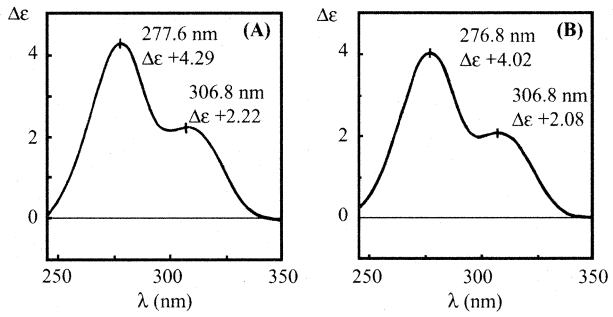


Fig. 2. CD Spectra for (A) (+)-Hongoquercin A and (B) **10** (c 1.5×10^{-3} M, $CHCl_3$).

same absolute configuration. This result is quite natural, because the synthesis of **10** started from **C** with an *S* absolute configuration. Subsequent acetylation of **10** with acetic anhydride in pyridine gave diacetate **11**, the phenolic acetyl group of which was selectively removed by treating with potassium carbonate in aqueous methanol to give (+)-hongoquercin B (**1**), mp 160–162°C and $[\alpha]_D^{24} = +163°$ (MeOH) [ref.1 mp 153–156°C and $[\alpha]_D^{25} = +160.2°$ (MeOH)]. Its IR, ^{1}H- and ^{13}C-NMR data were in good agreement with those reported for the natural product.[1] The overall yield of **1** was 34% based on **3** (7 steps), 25% based on **4** (7 steps) and 2% based on **C** (20 steps). Since the absolute configuration of starting material **C** is known to be *S*,[4] the present synthesis enables us to assign the absolute configuration as depicted in **1** to (+)-hongoquercin B.

In conclusion, (+)-hongoquercin B (**1**) was synthesized and shown to possess the same absolute configuration as that of (+)-hongoquercin A.

Experimental

Melting point (mp) data: Yanaco MP-S3, uncorrected values. IR: Hitachi Perkin Elmer 1640. ^{1}H-NMR: Jeol JNM-AL300 (300 MHz) and Jeol JNM-LA500 (500 MHz) (TMS at $\delta = 0.00$, or CH_3OD at $\delta = 3.30$ as internal standards). ^{13}C-NMR: Jeol JNM-AL300 (75 MHz) and Jeol JNM-LA500 (125 MHz) (TMS at $\delta = 0.0$, or methanol-d_4 at $\delta = 49.0$ as internal standards). Optical rotation: Jasco DIP-1000. CD spectrum: Jasco J-725.

Ethyl (4aR,6S,8aS)-3-[(6-benzyloxy-3,4,4a,5,6,7,8,8a-octahydro-2,5,5,8a-tetramethylnaphthyl)methyl]-2,4-dihydroxy-6-methylbenzoate [(+)-**6**]. Known (+)-**2** was prepared from 2-methylcyclohexane-1,3-dione.[3] (i) *Bromide* (+)-**3**:[3] Phosphorus tribromide (41 μl, 0.43 mmol) was added dropwise while stirring to a cooled suspension of (+)-**2** (400 mg, 1.22 mmol) in dry diethyl ether (4 ml) at −20°C under argon. After having been stirred for an additional 15 min, the resulting colorless solution was treated dropwise with methanol (0.1 ml) and water (2.0 ml), and the mixture was extracted with diethyl ether. The extract was successively washed with 5% aqueous sodium hydrogen carbonate, water and brine, dried with magnesium sulfate, and concentrated under reduced pressure to give 486 mg of crude (+)-**3**. This unstable colorless oil [(+)-**3**] was used immediately in the next step without further purification.

(ii) *Coupling product* **5**: Butyllithium (1.50 M in hexane, 1.08 ml, 1.62 mmol) was added dropwise to a cooled solution of **4** (946 mg, 1.62 mmol) in dry tetrahydrofuran (10 ml) at −78°C under argon. After standing for 30 min, the pale yellow solution was treated with copper (I) cyanide (291 mg, 3.25 mmol, dried at 120°C for 15 h under reduced pressure) in one portion. The suspension was warmed slowly to −10°C until almost all the copper (I) cyanide had dissolved and then recooled to −78°C. The mixture was treated dropwise with a solution of crude (+)-**3** (486 mg) in dry tetrahydrofuran (4 ml) and stirred for 2 h. The mixture was then poured into water and extracted with diethyl ether. The extract was successively washed with water and brine, dried with sodium sulfate, and concentrated under reduced pressure. The residue was chromatographed over silica gel (15 g). Elution with *n*-hexane/ethyl acetate (50:1) gave 998 mg of coupling product **5** contaminated with bis-SEM ether of ethyl orsellinate as a colorless oil.

(iii) *Dihydroxy ester* (+)-**6**: Crude **5** was dissolved in a mixture of ethanol (7 ml) and tetrahydrofuran (7 ml), and a sulfuric acid solution (0.3 ml in 3 ml of ethanol) was added at room temperature. The mixture was stirred for 15 h, neutralized to pH 7–8 with 5% aqueous sodium hydrogen carbonate, and extracted with chloroform. The extract was washed with brine, dried with sodium sulfate, and concentrated under reduced pressure. The residue was purified by chromatography over silica gel (15 g), eluting with *n*-hexane/ethyl acetate (40:1), and recrystallized from *n*-hexane to afford 455 mg (78% yield, 3 steps) of (+)-**6** as colorless plates, mp 127–128°C, $[\alpha]_D^{24}$ +148° (c 0.70, $CHCl_3$). IR ν_{max} (KBr) cm^{-1}: 3380 (vs, Ar-OH), 2980 (s, Ar-OH), 1640 (s, C=O), 1620 (s, Ar), 1580 (s, Ar), 1260 (s, C-O), 1250 (s, C-O), 1190 (s), 1020 (m, C-O). NMR δ_H (500 MHz, $CDCl_3$): 0.87 (3 H, s, 5-Me), 1.03 (3 H, s, 8a-Me), 1.07 (3 H, s, 5-Me), 1.17 (1 H, dd, $J = 12.5$, 2.2 Hz, 4a-H), 1.18 (1 H, ddd, $J = 13.5$, 13.5, 3.1 Hz, 8ax-H), 1.41 (3 H, t, $J = 7.2$ Hz, $CO_2CH_2CH_3$), 1.50 (1 H, dddd, $J = 13.5$, 13.5, 11.6, 3.3 Hz, 7ax-H), 1.60 (1 H, dddd, $J = 12.9$, 12.5, 10.7, 7.7 Hz, 4ax-H), 1.72 (1 H, ddd, $J = 13.5$, 3.5, 3.3 Hz, 8eq-H), 1.73 (3 H, s, 2-Me), 1.75 (1 H, m, 4eq-H), 1.80 (1 H, dddd, $J = 13.5$, 4.3, 3.5, 3.1 Hz, 7eq-H), 2.17 (2 H, m, 3-H), 2.47 (3 H, s, Ar-Me), 2.95 (1 H, dd, $J = 11.6$, 4.3 Hz, 6-H), 3.41 (1 H, d, $J = 17.5$ Hz, Ar-CH_2), 3.51 (1 H, d, $J = 17.5$ Hz, Ar-CH_2), 4.38 (1 H, d, $J = 11.9$ Hz, Ph-CH_2), 4.40 (2 H, q, $J = 7.2$ Hz, CO_2CH_2), 4.61 (1 H, d, $J = 11.9$ Hz, Ph-CH_2), 6.16 (1 H, s, Ar-H), 7.25 (1 H, m, Ph-H), 7.32 (4 H, m, Ph-H), 7.74 (1 H, s, Ar-OH), 12.39 (1 H, s, Ar-OH). NMR δ_C (125 MHz, $CDCl_3$): 14.3 (q, $CO_2CH_2CH_3$), 16.5 (q, 5-Me), 18.4 (t, Ar-CH_2), 19.9 (q, 8a-Me), 20.4 (q, 2-Me), 23.0 (t, 7-C), 24.2 (q+t, Ar-Me+4-C), 28.2 (q, 5-Me), 33.7 (t, 3-C), 33.8 (t, 8-C), 39.0 (s, 5-C), 39.3 (s, 8a-C), 51.2 (d, 4a-C), 61.2 (t, CO_2CH_2), 71.5 (t, Ph-CH_2), 86.3 (d, 6-C), 104.6 (s, 1′-C), 109.4 (s, 3′-C), 112.1 (d, 5′-C), 127.2 (d, *p*-Ph), 127.3 (d, *o*-Ph), 128.2 (d, *m*-Ph), 133.7 (s, 2-C), 139.43 (s, Ph), 139.45 (s, 1-C), 140.3 (s, 4′-C), 160.6 (s, 6′-C), 162.7 (s, 2′-C), 172.4 (s, C=O). *Anal.* Found: C, 75.76; H, 8.25%. Calcd.

for $C_{32}H_{42}O_5$: C, 75.86; H, 8.36%.

Ethyl (3S,4aR,6aR,12aR,12bS)-3-benzyloxy-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-11-hydroxy-4,4,6a,9,12b-pentamethylbenz[a]xanthene-10-carboxylate [(+)-**7**] and *ethyl (3S,4aR,6aR,12aR,12bS)-3-benzyloxy-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-11-hydroxy-4,4,6a,9,12b-pentamethylbenz[a]xanthene-8-carboxylate* [(+)-**8**]. Boron trifluoride diethyl etherate (30 μl, 0.24 mmol) was added dropwise while stirring to a solution of (+)-**6** (300 mg, 0.59 mmol) in dry dichloromethane (3 ml) at room temperature under argon. After having been stirred for an additional 2 h, the resulting pale yellow solution was diluted with water (2 ml) and extracted with dichloromethane. The extract was successively washed with water and brine, dried with sodium sulfate and concentrated under reduced pressure. The residue was recrystallized from ethanol to afford 168 mg (58%) of (+)-**7** as colorless powder, mp 150–151°C, $[\alpha]_D^{23}$ +165° (c 0.70, $CHCl_3$). IR ν_{max} (KBr) cm^{-1}: 3340 (w, Ar–OH), 2980 (s, Ar–OH), 1640 (s, C=O), 1580 (s, Ar), 1280 (s, C–O), 1270 (s, C–O), 1020 (m, C–O). NMR δ_H (500 MHz, $CDCl_3$): 0.87 (3 H, s, 4-Me), 0.94 (3 H, s, 12b-Me), 1.00 (1 H, dd, J=12.2, 2.0 Hz, 4a-H), 1.03 (3 H, s, 4-Me), 1.05 (1 H, m, 1ax-H), 1.19 (3 H, s, 6a-Me), 1.40 (3 H, t, J =7.2 Hz, $CO_2CH_2CH_3$), 1.43 (1 H, m, 5ax-H), 1.51 (1 H, dd, J=13.2, 5.2 Hz, 12a-H), 1.60 (1 H, m, 2ax-H), 1.65 (1 H, ddd, J=13.1, 12.5, 4.3 Hz, 6ax-H), 1.77 (1 H, m, 5eq-H), 1.89 (2 H, m, 1eq-H, 2eq-H), 2.07 (1 H, ddd, J=12.5, 3.1, 3.1 Hz, 6eq-H), 2.31 (1 H, dd, J=13.2, 16.8 Hz, 12ax-H), 2.46 (3 H, s, Ar–Me), 2.67 (1 H, dd, J=16.8, 5.2 Hz, 12eq-H), 2.95 (1 H, dd, J=11.6, 4.0 Hz, 3-H), 4.38 (2 H, q, J =7.2 Hz, CO_2CH_2), 4.43 (1 H, d, J =11.6 Hz, $PhCH_2$), 4.68 (1 H, d, J=11.6 Hz, $PhCH_2$), 6.17 (1 H, s, 8-H), 7.26 (1 H, m, Ph–H), 7.34 (4 H, m, Ph–H), 12.18 (1 H, s, Ar–OH). NMR δ_C (125 MHz, $CDCl_3$): 14.3 (q, $CO_2CH_2CH_3$), 15.0 (q, 4-Me), 16.6 (q, 12b-Me), 16.9 (t, 12-C), 19.4 (t, 5-C), 20.7 (q, 6a-Me), 22.8 (t, 2-C), 24.2 (q, Ar–Me), 28.3 (q, 4-Me), 36.7 (s, 4-C), 37.4 (t, 1-C), 39.0 (s, 12b-C), 40.9 (t, 6-C), 51.5 (d, 12a-C), 55.6 (d, 4a-C), 61.0 (t, CO_2CH_2), 71.5 (t, $PhCH_2$), 77.9 (s, 6a-C), 86.2 (d, 3-C), 104.0 (s, 11a-C), 107.8 (s, 10-C), 112.1 (d, 8-C), 127.2 (d, *p*-Ph), 127.4 (d, *o*-Ph), 128.2 (d, *m*-Ph), 139.4 (s, Ph), 140.1 (s, 9-C), 157.6 (s, 7a-C), 162.9 (s, 11-C), 172.3 (s, C=O). *Anal.* Found: C, 76.14; H, 8.47%. Calcd. for $C_{32}H_{42}O_5$: C, 75.86; H, 8.36%.

The mother liquor was concentrated under reduced pressure, and the resulting residue was purified by chromatography over silica gel with *n*-hexane/ethyl acetate (10:1), before being recrystallized from *n*-hexane and diethyl ether to afford 81 mg (27%) of (+)-**8** as colorless powder, mp 167–169°C, $[\alpha]_D^{22}$ +81° (c 0.70, $CHCl_3$). IR ν_{max} (KBr) cm^{-1}: 3380 (s, Ar–OH), 1680 (s, C=O), 1590 (s, Ar), 1290 (s, C–O), 1270 (s, C–O), 1090 (m, C–O), 1070 (m, C–O). NMR δ_H (500 MHz, $CDCl_3$): 0.87 (3 H, s, 4-Me), 0.91 (3 H, s, 12b-Me), 1.00 (1 H, dd, J=10.1, 3.1 Hz, 4a-H), 1.02 (3 H, s, 4-Me), 1.03 (1 H, ddd, J=13.4, 13.4, 3.7 Hz, 1ax-H), 1.18 (3 H, s, 6a-Me), 1.34 (3 H, t, J =7.3 Hz, $CO_2CH_2CH_3$), 1.42 (1 H, dddd, J=13.4, 13.4, 10.1, 3.1 Hz, 5ax-H), 1.58 (1 H, dd, J =13.1, 5.2 Hz, 12a-H), 1.59 (1 H, m, 2ax-H), 1.65 (1 H, ddd, J=13.4, 13.4, 4.3 Hz, 6ax-H), 1.75 (1 H, m, 5eq-H), 1.81 (1 H, ddd, J=13.4, 3.7, 3.7 Hz, 1eq-H), 1.88 (1 H, dddd, J=13.1, 4.3, 3.7, 3.7 Hz, 2eq-H), 2.01 (1 H, ddd, J=13.4, 3.1, 3.1 Hz, 6eq-H), 2.21 (3 H, s, Ar–Me), 2.31 (1 H, dd, J=16.5, 13.1 Hz, 12ax-H), 2.58 (1 H, dd, J=16.5, 5.2 Hz, 12eq-H), 2.95 (1 H, dd, J=11.9, 4.3 Hz, 3-H), 4.328 (1 H, q, J=7.3 Hz, CO_2CH_2), 4.331 (1 H, q, J=7.3 Hz, CO_2CH_2), 4.44 (1 H, d, J=11.6 Hz, $PhCH_2$), 4.67 (1 H, d, J=11.6 Hz, $PhCH_2$), 4.93 (1 H, s, Ar–OH), 6.14 (1 H, s-like, 10-H), 7.26 (1 H, m, Ph–H), 7.34 (4 H, m, Ph–H). NMR δ_C (125 MHz, $CDCl_3$): 14.4 (q, $CO_2CH_2CH_3$), 14.8 (q, 4-Me), 16.5 (q, 12b-Me), 16.9 (t, 12-C), 19.30 (q, Ar–Me), 19.33 (t, 5-C), 20.6 (q, 6a-Me), 22.8 (t, 2-C), 28.3 (q, 4-Me), 36.6 (s, 4-C), 37.3 (t, 1-C), 39.0 (s, 12b-C), 40.6 (t, 6-C), 51.1 (d, 12a-C), 55.6 (d, 4a-C), 60.7 (t, CO_2CH_2), 71.6 (t, $PhCH_2$), 77.2 (s, 6a-C), 86.3 (d, 3-C), 107.2 (s, 8-C), 107.9 (s, 11a-C), 115.8 (d, 10-C), 127.3 (d, *p*-Ph), 127.4 (d, *o*-Ph), 128.2 (d, *m*-Ph), 135.0 (s, 9-C), 139.3 (s, Ph), 152.0 (s, 11-C), 154.9 (s, 7a-C), 168.9 (s, C=O). *Anal.* Found: C, 75.68; H, 8.49%. Calcd. for $C_{32}H_{42}O_5$: C, 75.86; H, 8.36%.

Ethyl (3S,4aR,6aR,12aR,12bS)-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-3,11-dihydroxy-4,4,6a,9,12b-pentamethylbenz[a]xanthene-10-carboxylate [(+)-**9**]. To a solution of (+)-**7** (205 mg, 0.40 mmol) in ethyl acetate (4.1 ml) was added 10% Pd–C (8 mg) at room temp. The mixture was stirred at room temp. under hydrogen for 11 h, and then the Pd catalyst was filtered off. The resulting filtrate was concentrated under reduced pressure, and the residue was recrystallized from pentane-ethyl acetate to afford 156 mg (93%) of (+)-**9** as colorless powder, mp 189–190°C, $[\alpha]_D^{24}$ +129° (c 0.60, $CHCl_3$). IR ν_{max} (KBr) cm^{-1}: 3550 (w, Ar–OH), 3470 (br, 3-OH), 1640 (s, C=O), 1580 (s, Ar), 1280 (s, C–O), 1170 (m, C–O), 1040 (m, C–O), 1020 (m, C–O). NMR δ_H (500 MHz, $CDCl_3$): 0.82 (3 H, s, 4-Me), 0.93 (3 H, s, 12b-Me), 1.01 (1 H, dd, J=12.2, 2.2 Hz, 4a-H), 1.03 (3 H, s, 4-Me), 1.12 (1 H, ddd, J=13.2, 13.1, 4.3 Hz, 1ax-H), 1.19 (3 H, s, 6a-Me), 1.40 (3 H, t, J=7.0 Hz, $CO_2CH_2CH_3$), 1.45 (1 H, m, 5ax-H), 1.52 (1 H, dd, J =13.2, 5.2 Hz, 12a-H), 1.58 (1 H, br, 3-OH), 1.63-1.73 (3 H, m, 2ax-H, 2eq-H, 6ax-H), 1.78 (1 H, m, 5eq-H), 1.85 (1 H, ddd, J=13.1, 4.6, 4.6 Hz, 1eq-H), 2.08 (1 H, ddd, J=12.8, 3.4, 3.1 Hz, 6eq-H), 2.31 (1 H, dd, J=16.8, 13.2 Hz, 12ax-H), 2.46 (3 H, s, Ar–Me), 2.67 (1 H, dd, J=16.8, 5.2 Hz, 12eq-H),

3.25 (1 H, dd, J=11.6, 4.6 Hz, 3-H), 4.38 (2 H, q, J =7.0 Hz, CO_2CH_2), 6.17 (1 H, s, 8-H), 12.18 (1 H, s, 11-OH). NMR δ_C (125 MHz, $CDCl_3$): 14.3 (q, $CO_2CH_2CH_3$), 15.0 (q, 12b-Me), 15.5 (q, 4-Me), 16.8 (t, 12-C), 19.4 (t, 5-C), 20.6 (q, 6a-Me), 24.2 (q, Ar-Me), 27.2 (t, 2-C), 28.1 (q, 4-Me), 36.8 (s, 4-C), 37.5 (t, 1-C), 38.8 (s, 12b-C), 40.8 (t, 6-C), 51.5 (d, 12a-C), 55.1 (d, 4a-C), 61.1 (t, CO_2CH_2), 77.8 (s, 6a-C), 78.7 (d, 3-C), 104.1 (s, 11a-C), 107.8 (s, 10-C), 112.1 (d, 8-C), 140.1 (s, 9-C), 157.6 (s, 7a-C), 162.9 (s, 11-C), 172.3 (s, C=O). *Anal.* Found: C, 71.88; H, 8.72%. Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71%.

(3S,4aR,6aR,12aR,12bS)-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-3,11-dihydroxy-4,4,6a,9,12b-pentamethylbenz[a]xanthene-10-carboxylic Acid [(+)-**10**]. To a solution of (+)-**9** (155 mg, 0.37 mmol) in a mixture of methanol (1 ml) and tetrahydrofuran (1.5 ml) was added a potassium hydroxide solution (52 mg, 85 %, 0.78 mmol, in 1 ml of water), and the mixture was stirred for 4 h at reflux temperature. The reaction mixture was cooled and acidified to pH 2–3, before being extracted with dichloromethane. The extract was successively washed with water and brine, dried with sodium sulfate and concentrated under reduced pressure. The residue was chromatographed over silica gel (4.0 g), eluting with chloroform/methanol (20:1), to afford 138 mg (96%) of (+)-**10** as colorless powder, mp 150–152°C, $[\alpha]_D^{24}$ +139° (c 0.30, MeOH). CD (c 1.50×10^{-3} M, $CHCl_3$) $\Delta\varepsilon$ (λ, nm): +4.02 (277), +2.08 (307). IR ν_{max} (KBr) cm^{-1}: 3560 (m, Ar-OH), 3500 (m, 3-OH), 3280 (br, CO_2H), 2640 (m, CO_2H), 1610 (s, C=O), 1580 (s, Ar), 1030 (s, C-O), 1020 (s, C-O). NMR δ_H (500 MHz, CD_3OD): 0.81 (3 H, s, 4-Me), 0.94 (3 H, s, 12b-Me), 1.00 (3 H, s, 4-Me), 1.02 (1 H, dd, J=11.9, 2.1 Hz, 4a-H), 1.14 (1 H, m, 1ax-H), 1.17 (3 H, s, 6a-Me), 1.47 (1 H, dd, J=13.3, 5.0 Hz, 12a-H), 1.48 (1 H, dddd, J =13.5, 13.5, 11.9, 3.1 Hz, 5ax-H), 1.63 (1 H, m, 6ax-H), 1.65 (1 H, m, 2ax-H), 1.69 (1 H, m, 2eq-H), 1.76 (1 H, m, 1eq-H), 1.78 (1 H, m, 5eq-H), 2.03 (1 H, ddd, J=12.5, 3.1, 3.1 Hz, 6eq-H), 2.26 (1 H, dd, J=16.6, 13.3 Hz, 12ax-H), 2.44 (3 H, s, Ar-Me), 2.62 (1 H, dd, J=16.6, 5.0 Hz, 12eq-H), 3.19 (1 H, dd, J=11.3, 5.0 Hz, 3-H), 6.09 (1 H, s, 8-H). NMR δ_C (125 MHz, CD_3OD): 15.4 (q, 12b-Me), 16.2 (q, 4-Me), 17.8 (t, 12-C), 20.5 (t, 5-C), 21.0 (q, 6a-Me), 24.2 (q, Ar-Me), 27.9 (t, 2-C), 28.7 (q, 4-Me), 37.8 (s, 4-C), 38.8 (t, 1-C), 39.9 (s, 12b-C), 42.1 (t, 6-C), 52.9 (d, 12a-C), 56.5 (d, 4a-C), 78.8 (s, 6a-C), 79.4 (d, 3-C), 104.9 (s, 11a-C), 108.7 (s, 10-C), 112.8 (d, 8-C), 141.8 (s, 9-C), 158.9 (s, 7a-C), 164.5 (s, 11-C), 175.6 (s, C=O). *Anal.* Found: C, 70.72; H, 8.23%. Calcd. for $C_{23}H_{32}O_5$: C, 71.11; H, 8.30%.

(+)-Hongoquercin B (**1**). To a solution of (+)-**10** (65 mg, 0.17 mmol) in pyridine (0.6 ml) was added acetic anhydride (102 μl, 1.08 mmol) at room temp. After having been stirred for 24 h, the resulting pale yellow solution was diluted with water (2 ml), and extracted with chloroform. The extract was successively washed with 1 N hydrochloric acid, a sat. aq. $CuSO_4$ solution, water and brine, dried with sodium sulfate and concentrated under reduced pressure. The residue containing **11** (82 mg) was dissolved in methanol (2 ml) and water (0.3 ml), and to this mixture was added potassium carbonate (43 mg, 0.31 mmol) at room temp. After having been stirred for an additional 5 h, the resulting pale yellow solution was acidified to pH 2–3, and extracted with chloroform. The extract was successively washed with water and brine, dried with sodium sulfate and concentrated under reduced pressure. The resulting residue was chromatographed over silica gel (6 g), eluting with chloroform/ethanol (200:1), to afford 64 mg (89%) of (+)-**1** as colorless powder, mp 160–162°C [ref. 1: 153–156°C], $[\alpha]_D^{24}$ +163° (c 0.53, MeOH) [ref. 1: $[\alpha]_D^{25}$ +160.2° (c 0.52, MeOH)]. IR ν_{max} (KBr) cm^{-1}: 3440 (br, CO_2H), 2970 (s, Ar-OH), 1740 (s, $OCOCH_3$: this is not mentioned in ref.[1]), 1620 (s, C=O), 1580 (s, Ar), 1450 (s), 1370 (s), 1270 (s), 1250 (s), 1180 (m), 1130 (s), 1030 (m, C-O), 1010 (m, C-O). NMR δ_H(500 MHz, $CDCl_3$): 0.90 (3 H, s, 4-Me), 0.91 (3 H, s, 12b-Me), 0.96 (3 H, s, 4-Me), 1.10 (1 H, dd, J=12.2, 1.8 Hz, 4a-H), 1.19 (1 H, ddd, J=13.2, 13.2, 3.7 Hz, 1ax-H), 1.20 (3 H, s, 6a-Me), 1.44 (1 H, m, 5ax-H), 1.53 (1 H, dd, J=13.1, 4.9 Hz, 12a-H), 1.64–1.80 (4 H, m, 2ax, 2eq, 5eq, 6ax-H), 1.86 (1 H, ddd, J=13.2, 3.4, 3.4 Hz, 1eq-H), 2.07 (3 H, s, $COCH_3$), 2.08 (1 H, ddd, J=12.5, 3.1, 3.1 Hz, 6eq-H), 2.31 (1 H, dd, J=16.8, 13.1 Hz, 12ax-H), 2.52 (3 H, s, Ar-Me), 2.67 (1 H, dd, J= 16.8, 4.9 Hz, 12eq-H), 4.52 (1 H, dd, J=11.6, 4.9 Hz, 3-H), 6.21 (1 H, s, 8-H), 11.85 (1 H, s, Ar-OH). NMR δ_C (75 MHz, $CDCl_3$): 15.0, 16.6, 16.8, 19.3, 20.6, 21.3, 23.5, 24.1, 28.0, 36.6, 37.1, 37.7, 40.6, 51.2, 55.1, 77.9, 80.6, 102.9, 107.7, 112.6, 141.5, 158.5, 163.8, 171.1, 176.1. *Anal.* Found: C, 69.46; H, 7.94%. Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

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